Pergamon

Tetrahedron Letters 43 (2002) 3845–3847

TETRAHEDRON LETTERS

Taibaihenryiin C, a diterpenoid with a novel skeleton from *Isodon henryi*

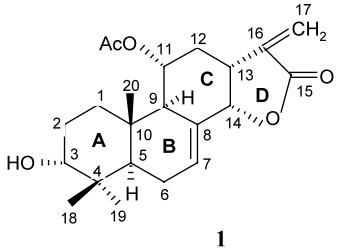
Bao-Lin Li,[a,*] Yuan-Jiang Pan[b] and Kai-Bei Yu[c]

[a]*School of Chemistry and Material Science, Shaanxi Normal University, Xi'an, Shaanxi 710062, China*
[b]*Department of Chemistry, Zhejiang University, Hangzhou, Zhejiang 310027, China*
[c]*Chengdu Institute of Organic Chemistry, Academia Sinica, Chengdu, Sichuan 610041, China*

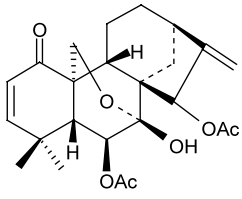
Received 5 February 2002; revised 13 February 2002; accepted 5 April 2002

Abstract—A diterpenoid with a novel skeleton, taibaihenryiin C, along with four known compounds, odonicin, rabdosianin B, wikestroemioidin C and eupafolin were isolated from an ethanol extract of the leaves and new branches of *Isodon henryi* (Hemsl.) Kudo (Labiatae) and its structure was elucidated on the basis of spectroscopic data and X-ray crystallography.

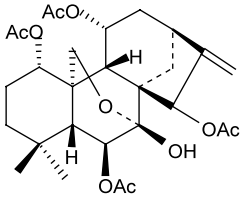
In past studies, a large number of structurally interesting diterpenoids with various biological activities, such as anti-HIV,[1] antitumor and inhibition of insect growth,[2] were discovered from medicinal plants of the genus *Isodon*. Plants of this genus have been used for gastrointestinal disorders and as antitumor and antiphlogistic agents in Chinese traditional medicine.[3] Three major structural types, the *ent*-kaurene type, the 6,7-B-*seco*-*ent*-kaurene type and the 8,9-*seco*-*ent*-kaurene type and three minor structural types, 6-*epi*-*ent*-gibberelene, *ent*-isopimanthrene and abietene type have been found in these *Isodon* diterpenoids.[4] Recently, our investigations of the chemical constituents of a specimen of *Isodon henryi* collected on Taibai Mountain, Shaanxi Province, PR China, yielded a diterpenoid with a novel skeleton, taibaihenryiin C **1**, together with four known compounds, odonicin **2**, rabdosianin B **3**, wikestroemioidin C **4** and eupafolin **5**.



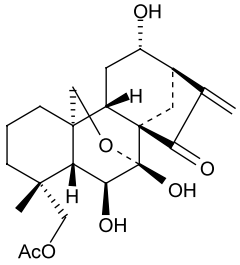
1



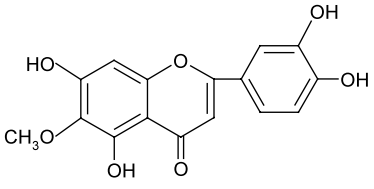
2



3



4



5

Taibaihenryiin C **1** was obtained from the dried powdered leaves and new branches extract (0.0025%)[5] as irregular hexagonal colorless crystals (mp 255–256.5°C), with $[\alpha]_D^{25}$ −111.3 ($c=0.55$, $CHCl_3$) and had the molecular formula $C_{22}H_{30}O_5$ as revealed by the FABMS [m/z: 381(M+Li)$^+$ and 397(M+Na)$^+$], the X-ray single-crystal structure determination, and elemental analysis [found: C, 70.5%; H, 7.8% (calcd C, 70.6%; H, 8.0%)]. Its IR spectrum showed characteristic absorption bands for the hydroxyl group, the carbonyl

Keywords: taibaihenryiin C; diterpenoid; *Isodon henryi*; Labiatae.

* Corresponding author. Tel.: +86-29-5303858; fax: +86-29-5307774; e-mail: baolinli@snnu.edu.cn

0040-4039/02/$ - see front matter
PII: S0040-4039(02)00677-9

group and double bonds (3537, 1754, 1715, 1666 cm^{-1}), and these assignments were confirmed by its ^{13}C and ^{1}H NMR spectral data (see Table 1) (δ 170.6, 170.8 ppm; 132.7, 130.2 ppm; 142.6, 120.1 ppm and δ 6.08, 6.13, 5.49 ppm). The ^{1}H, ^{13}C and HMQC NMR spectra of **1** showed signals for three methyl groups, four methylene groups, six methine groups, two quaternary carbons and four olefinic carbons including an *exo*-methylene, one acetoxyl group and one ester carbonyl carbon.

Since four out of eight degrees of unsaturation were accounted for, taibaihenryiin C **1** was inferred to contain four rings. In the HMBC spectrum of **1** (see Table 1), the signals at δ 1.59 (H-2α) and 1.63 (H-2β) showed correlation with the signals at δ 25.1 (t, C-1), 75.8 (d, C-3) and 37.4 (s, C-4); the signal at δ 1.80 (1H, dd, $J=12.1$, 4.8 Hz, H-5β) correlated with the signals at δ 37.4 (s, C-4), 35.4 (s, C-10), 14.3 (q, C-20) and 25.1 (t, C-1); the signals at δ 0.96 (3H, H-18) and 0.92 (3H, H-19) exhibited cross peaks with both signals at δ 37.4 and 43.1 (d, C-5), respectively. These indicated the presence of structure unit ring A with two methyl groups at C-4 and a methyl group at C-10 (see Fig. 1). Ring B was formed by connecting the structural unit -CH_2-CH=C-CH- through C-5 and C-10, which was judged from the HMBC correlation from the two proton signals at δ 2.02 (1H, m, H-6α) and 2.09 (1H, m, H-6β) to the carbon signals at δ 43.1 (d, C-5), 132.7 (d, C-7) and 130.2 (s, C-8), and from the proton signal at δ 2.40 (1H, br s, H-9β) to the carbon signals at δ 35.4 (s, C-10), 130.2 (s, C-8), 132.7 (d, C-7), 69.2 (d, C-11) and 14.3 (s, C-20). HMBC correlations from the proton signal at δ 1.71 (1H, dd, $J=7.3$, 2.2 Hz, H-12α) to the carbon signal at δ 36.9 (d, C-13); from δ 2.03 (1H, m, H-12β) to δ 51.0 (d, C-9), 69.2 (d, C-11) and 81.8 (d, C-14); from δ 3.33 (1H, m, H-13α) to δ 69.2 (d, C-11) and 33.9 (t, C-12), and from δ 4.94 (1H, d, $J=8.1$ Hz, H-14α) to δ 130.2 (s, C-8), 132.7 (d, C-7), suggested that ring C was constructed by connecting the structural unit -CH-CH_2-CH-CH- through C-9 and C-8. Meanwhile, its ^{13}C NMR spectrum showed signals for two ester carbonyl carbons (δ 170.6 and 170.8 ppm),

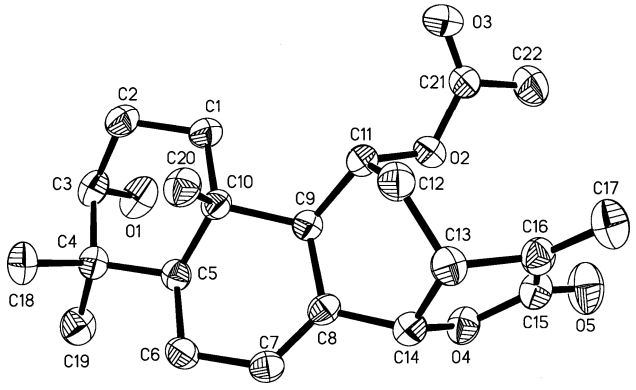


Figure 1. X-Ray crystal structure of **1**.

Table 1. The ^{1}H, ^{13}C NMR, HMBC and ^{1}H–^{1}H COSY spectral data of taibaihenryiin C in CD_3Cl[a]

Position (H)	δ_H, mult., intgr. (*J*, Hz)	δ_c (mult.)[b]	HMBC (carbon)[c]	^{1}H–^{1}H COSY
1α	1.63, m, 1H	25.1 (t)	10, 4	3α
1β	1.90, overlap, 1H		5	3α
2α	1.59, m, 1H	30.6 (t)	(1), (3), 4, 5, 10, 20	n.o.[d]
2β	1.63, overlap, 1H		(1), (3), 4, 5, 10, 20	3α
3α	3.47, t, 1H (2.5)	75.8 (d)	(2), (4), 5, 19	1β, 1α, 2β
4		37.4 (s)		
5β	1.80, dd, 1H (12.1, 4.8)	43.1 (d)	1, (4), 9, (10), 20	n.o.
6α	2.02, m, 1H	23.6 (t)	(5), (7), 8	7
6β	2.09, m, 1H		(5), (7), 8	7
7	6.08, dd, 1H (4.8, 2.2)	132.7 (d)	5, (6), 9, 14	6α, 6β, 9β
8		130.2 (s)		
9β	2.40, br s, 1H	51.0 (d)	(8), 7, (10), (11), 20	7, 11α, 12β
10		35.4 (s)		
11α	5.14, t, 1H (1.6)	69.2 (d)	8, 10, 13, OAc (170.6 ppm)	9β, 12β
12α	1.71, dd, 1H (7.3, 2.2)	33.9 (t)	(13), 16	13α
12β	2.03, m, 1H		9, (11), 14	9β, 11α, 13α
13α	3.33, m, 1H	36.7 (d)	11, (12), 15, 16	12α, 12β, 14α, 17a, 17b
14α	4.94, d, 1H (8.1)	81.8 (d)	5, 7, (8), 12	13α
15		170.8 (s)		
16		142.6 (s)		
17a	6.13, d, 1H (2.2)	120.1 (t)	13, 15, (16)	13α
17b	5.49, d, 1H (1.9)		13, 15, (16)	13α
18	0.96, s, 3H	28.2 (q)	(4), 5, 19	n.o.
19	0.92, s, 3H	22.5 (q)	(4), 5, 19	n.o.
20	0.82, s, 3H	14.3 (q)	2, 5, 9, (10)	n.o.
OAc		170.6 (s)		
	1.91, s, 3H	21.0 (q)		

[a] The chemical shift values are in parts per million relative to TMS. The spectra were recorded at 500 MHz at room temperature.
[b] The ^{13}C NMR multiplicities were obtained from the HMQC spectrum.
[c] Two-bond correlations are indicated in parentheses.
[d] n.o. indicates no clear correlations.

but there was only one signal of the methyl of an acetoxyl group (δ 1.91, s, 3H) in the ^{1}H NMR spectrum, which revealed that a lactone structure was present in **1**. Connecting C-16 and the oxygen atom of the ester group to ring C through C-13 and C-14, respectively, constructed ring D with an *exo*-methylene γ-lactone structure. This was deduced from the HMBC correlations from the signal at δ 3.33 (1H, m, H-13α) to δ 142.6 (s, C-16) and 170.8 (s, C-15) and from δ 6.13 (1H, d, J=2.2 Hz, H-17a) and 5.49 (1H, d, J=1.9 Hz, H-17b) to δ 142.6 (s, C-16), 36.7 (d, C-13) and 170.8 (s, C-15). This evidence indicated that compound **1** was a diterpenoid with a novel skeleton containing a γ-lactone. The hydroxyl group and the acetoxyl group in **1** were located at C-3 and C-11 resulting from the signals at δ 3.47 (1H, t, J=2.5 Hz, H-3α), 75.8 (d, C-3) in the ^{1}H, ^{13}C and HMQC NMR spectra of **1**, and the HMBC correlation from the proton signal at δ 5.14 (1H, t, J=1.6 Hz, H-11α) to the carbon signal at δ 170.6 (s, AcO), respectively. The above conclusions were further confirmed by the ^{1}H–^{1}H COSY spectral data of **1** (see Table 1). Thus, the structure of taibaihenryiin C was elucidated to be **1**.

The relative stereochemistry of **1** was determined as shown in Fig. 1 by single-crystal X-ray diffraction analysis.[6] The hydroxyl group at C-3 and the acetoxyl group at C-11 are in the β-orientations, respectively. Ring A is in a chair conformation, and rings B and C approximate in boat conformations. C-14 diverges slightly from the common plane of C-13, C-16, C-15 and O-4, so ring D approximates to an envelope conformation.

Compounds **2**, **3** and **4** were identified as the diterpeneoids, odonicin, rabdosianin B and wikestroemioidin C, respectively; compound **5** was shown to be the flavone eupafolin, by comparison of the physical and ^{13}C NMR data with that reported.[7]

Acknowledgements

We are grateful for the financial support from the Natural Science Foundation of Shaanxi Province. We would like to thank Professor Xianhua Tian, Life Science College, Shaanxi Normal University (PR China), for identification of the plant samples.

References

1. (a) Wu, Y. C.; Hung, Y. C.; Cheng, F. R.; Cosentino, M.; Wang, H. K.; Lee, K. H. *J. Nat. Prod.* **1996**, *59*, 635–637; (b) Chen, K.; Shi, Q.; Fujioka, T.; Nakano, T.; Hu, C. Q.; Jin, J. Q.; Kilkuskie, R. E.; Lee, K. H. *Bioorg. Med. Chem.* **1995**, *3*, 1345–1348.
2. Fujita, T.; Takeda, Y.; Sun, H. D.; Minami, Y.; Marunaka, T.; Takeda, S.; Yamada, Y.; Togo, T. *Planta Med.* **1988**, 414–417.
3. Wu, S. H.; Zhang, H. J.; Chen, Y. P.; Lin, Z. W.; Snu, H. D. *Phytochemistry* **1993**, *34*, 1099–1102.
4. (a) Guo, Y. W.; Chen, P. Y. *Zhong Cao Yao* **1991**, *22*, 371–375; (b) Fujita, E.; Node, M. *Prog. Chem. Org. Nat. Prod.* **1984**, *46*, 77–158.
5. The dried powdered leaves and new branches of *Isodon henryi* (5.0 kg) were extracted with 95% EtOH (15 L×3) at room temperature for 7 days. After removal of the solvent in vacuo, the residue was partitioned in H_2O and extracted with petroleum ether (3 L×3) and EtOAc (3 L×3), respectively. The EtOAc extract (122 g) was subjected to column chromatography on silica gel (2 kg, 200–300 mesh), eluting with $CHCl_3$ and increasing proportions of Me_2CO ($CHCl_3$/Me_2CO: from 10:0 to 0:10). Fractions were combined by monitoring with TLC. All components were further purified by column chromatography and preparative TLC on silica gel to give **2** (113 mg, 0.0023%), **3** (194 mg, 0.0039%), **1** (126 mg, 0.0025%), **4** (114 mg, 0.0023%) and **5** (623 mg, 0.012%), respectively.
6. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 182951. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB12 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].
7. (a) Wang, X. R.; Hu, H. P.; Wang, H. P. *Zhong Cao Yao* **1994**, *25*, 115–117; (b) Ochi, M.; Okamura, M.; Kotsuki, H.; Miura, I.; Kubo, I.; Kubota, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2786–2789; (c) Wu, S. H.; Zhang, H. J.; Chen, Y. P.; Lin, Z. W.; Sun, H. D. *Phytochemistry* **1993**, *34*, 1099–1102.