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DITERPENOIDS FROM *ISODON ERIOCALYX*

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Key Word Index—*Isodon eriocalyx*; Labiatae; leaves; structure determination; diterpenoids; maoecrystal P.

Abstract—A new *ent*-kaurane diterpenoid named maoecrystal P and a known compound coetsoidin A were isolated from the dried leaves of *Isodon eriocalyx*. They represent the only two *ent*-kaurane diterpenoids possessing an α,β-unsaturated ketone functional group in ring B to be isolated from *Isodon* genus plants so far. The structures were elucidated on the basis of spectroscopic methods. © 1997 Elsevier Science Ltd

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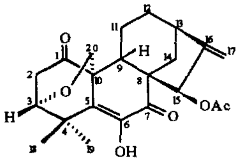
INTRODUCTION

Isodon eriocalyx (Dunn.) Hara is a perennial herb or shrub which is widely distributed in South-west China. It has long been used in folk medicine to cure sore throats inflammation and interdigital disease [1]. In our preceding paper, we isolated three new diterpenoids from the dried leaves of *I. eriocalyx* (Dunn.) Hara collected in Jiangchuan County, Yunnan Province, Peoples Republic of China [2].

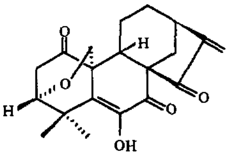
Further investigation of the same plant has led to the isolation and structural determination of one new *ent*-kaurane diterpenoid named maoecrystal P and a known compound coetsoidin A. They are the only two *ent*-kauranes possessing an α,β-unsaturated ketone functional group in ring B to be isolated from *Isodon* spp so far.

RESULTS AND DISCUSSION

Coetsoidin A (**1**), the first example of an *ent*-kaurane possessing an α,β-unsaturated ketone function in ring B was first isolated from *coetsoides* C. Y. Wu by X. F. Wang in 1989 [3]. Its structure was established unambiguously by spectroscopic and X-ray diffraction analysis. Coetsoidin A (**1**) was also obtained from *I. eriocalyx* by us. The ^{1}H NMR and ^{13}C NMR data of **1** were consistent with those reported previously, except that the assignments of C-5, 6, 9 and 13 were uncorrect. This was proved by 2D NMR.



Coetsoidin A (1)



2

In the ^{1}H-^{13}C COSY spectrum of **1**, the proton signals ascribable to H-9β (δ 3.72) and H-13 α (δ 2.66), both of which were determined by ^{1}H-^{1}H COSY spectrum, showed correlation with C-9 (δ 28.0) and C-13 (δ 41.6), respectively. Thus, the carbon signal attributed to C-9 (δ 41.6) and C-13 (δ 28.0) in the literature should be interchanged. Moreover, among the long-range couplings observed in the COLOC spectrum, the proton signals for H-3, Me-18 and Me-19 showed significant correlations with C-5 (δ 133.1). Thus the signals originally attributed to C-6 (δ 133.1) and C-5 (δ 146.1) also should be interchanged. The revised assignments of the ^{13}C NMR signals are listed in Table 1.

The ^{13}C NMR spectra of Maoecrystal P (**2**) showed the presence of two methyls, five methylenes (including one oxygenated methylene), three methines, three quaternary carbons, four olefinic carbons and three carbonyl carbons. These facts, together with the consideration of the EI mass spectrum ($[M]^+ = m/z$ 342) revealed that **2** had a molecular formula of $C_{20}H_{22}O_5$.

A comparison of the ^{1}H and ^{13}C NMR spectral data of **2** with those of **1** indicated that **2** was quite similar to **1** except for ring D. The carbon signal assigned to C-15 at δ 76.4 in **1** was replaced by a ketonic signal at δ 203.4 in **2** and the proton signal ascribable to H-15 α at δ 6.83 (1H, *t*, $J = 2.0$ Hz) in **1** was absent in **2**. In addition, the signals attributed to the acetyl group in **1** were also absent in **2**. All these facts are consistent with the structure of **2** being 6-hydroxy-3α,20-epoxy-*ent*-kaur-16-en-5,6-ethenylene-1,7,15-trione.

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Table 1. ^{13}C NMR data of compounds **1** and **2** (100 MHz, δ in ppm with reference to the signal C_5D_5N)

C	1	2
1	206.2 *s*	205.4 *s*
2	42.0 *t*	41.9 *t*
3	77.9 *d*	78.0 *d*
4	40.8 *s*	40.9 *s*
5	133.1 *s*	133.4 *s*
6	146.1 *s*	147.0 *s*
7	194.4 *s*	192.9 *s*
8	54.4 *s*	59.7 *s*
9	28.0 *d*	32.6 *d*
10	53.9 *s*	54.9 *s*
11	19.7 *t*	19.6 *t*
12	32.1 *d*	30.8 *d*
13	41.6 *d*	38.0 *d*
14	38.1 *t*	38.1 *t*
15	76.4 *d*	203.4 *s*
16	152.5 *s*	149.0 *s*
17	108.5 *t*	116.0 *t*
18	23.6 *q*	23.4 *q*
19	21.9 *q*	22.0 *q*
20	67.4 *t*	66.9 *t*
OAc	170.5 *s*	
	20.7 *t*	

Compound **2** is the second example of an *ent*-kaurane diterpenoid possessing an α,β-unsaturated ketone functional group in ring B isolated from *Isodon* species.

EXPERIMENTAL

General. Mp: uncorr.; MS: VG Autospec-3000 spectrometer; NMR: 400 (^1H) and 100 (^{13}C) MHz, C_5D_5N, the solvent signals as int. ref.

Plant material. Plant material was collected in Jiangchuan County, Yunnan Province, Peoples Republic of China, in 1994 and identified as *Isodon eriocalyx* (Dunn.) Hara by Prof. X.-W. Li. A voucher specimen is kept in the Herbarium of Kunming Institute of Botany, Academic Sinica, Kunming, Yunnan, Peoples Republic of China.

Extraction and isolation. Dried powdered leaves of *I. eriocalyx* (11.9 kg) were extracted with MeOH (4 × 40 l) under reflux and then conc *in vacuo* to give a crude extract (978 g). The extract was dissolved in H_2O containing 40% EtOH and then defatted with petrol (60–90°). After the removal of EtOH, the residue was extracted with EtOAc. The EtOAc extract (395 g) was chromatographed on a silica gel column (1.6 kg, 200–300 mesh) eluting with $CHCl_3$ containing increasing amounts of Me_2CO to yield seven frs. Frs I, II and III were submitted to MCI gel to remove green pigments. Then both frs II and III were subjected to silica gel H CC. Repeated elution with $CHCl_3$–cyclohexane–*iso*-PrOH followed by recrystallization finally afforded compounds **1** (50 mg) and **2** (24 mg).

Coetsoidin A (**1**). $C_{22}H_{26}O_6$, colourless crystals (from MeOH), mp 180–182°. IR ν_{max}^{KBr} cm^{-1}: 3260, 2960, 2940, 1723, 1650, 1622, 1450, 1360, 1310, 1224, 1153, 1040, 890 and 665; UV λ_{max}^{MeOH} nm (log ε): 280.0 (4.00), 302.5 (3.60), 313.0 (3.62) and 320.5 (3.50, sh); EIMS (70 eV)

Table 2. ^1H NMR data of compounds **1** and **2** (400 MHz, δ in ppm with reference to the signal of C_5D_5N)

H	1	2	^1H-^1H COSY
2α	3.03 (*dd*, 3.2, 19.2)	2.93 (*dd*, 3.2, 19.6)	3β
2β	2.89 (*dd*, 3.2, 19.2)	2.85 (*dd*, 3.2, 19.6)	3β
3β	3.86 (*br s*)	3.84 (*t*, 3.2)	2α, 2β
9β	3.72 (*d*, 7.6)	3.48 (*d*, 8.0)	11β
11α	1.43–1.47 (*m*, overlap)	1.42–1.50 (*m*, overlap)	11β, 12α
11β	2.19 (*m*)	1.71 (*m*)	9β, 11α, 12α, 12β
12α	1.28 (*m*)	1.42–1.50 (*m*, overlap)	11α, 11β, 12β, 13α
12β	1.43–1.47 (*m*, overlap)	1.42–1.50 (*m*, overlap)	11β, 12α, 13α
13α	2.66 (*br s*)	2.95 (*br s*)	12α, 12β, 14β
14α	1.80 (*d*, 12.0)	2.12 (*d*, 11.6)	14β
14β	1.54 (*dd*, 12.0, 4.8)	1.98 (*dd*, 11.6, 4.8)	13α, 14α
15α	6.83 (*t*, 2.0)		
17b	5.02 (*br s*)	6.09 (*br s*)	17a
17a	5.24 (*br s*)	5.23 (*br s*)	17b
18-Me	1.80 (*s*)	1.78 (*s*)	
19-Me	1.96 (*s*)	1.29 (*s*)	
20b	4.36 (*d*, 8.8)	4.75 (*d*, 8.8)	20a
20a	4.47 (*d*, 8.8)	4.33 (*d*, 8.8)	20b
OAc	1.96 (*s*)		
OH-6	11.00 (*s*)	11.25 (*s*)	

m/z (rel. int.): 386 $[M]^+$ (100), 356 (17), 344 (34), 326 (6), 302 (26), 284 (49), 256 (59), 228 (21), 215 (24) and 91 (28); ^{13}C and ^{1}H NMR: Tables 1 and 2.

Maoecrystal P (**2**). $C_{20}H_{22}O_5$, colourless crystals (from MeOH), mp 234–236°. $[\alpha]_D^{25}$ −141.7° ($CHCl_3$, c 0.30); IR ν_{max}^{KBr} cm^{-1}: 3355, 2914, 1720, 1640, 1617, 1440, 1350, 1288, 1200, 1150, 1050, 933 and 917; UV λ_{max}^{MeOH} (log ε): 238.0 (3.72), 270.5 (3.84, sh), 281.5 (3.93), 301.0 (3.54), 312.0 (3.59) and 320.5 (3.46, inf); EIMS (70 eV) m/z (rel. int.): 342 $[M]^+$ (100), 312 (32), 300 (95), 272 (87), 244 (48), 215 (42), 189 (38), 128 (34), 115 (40), 105 (43), 91 (61) and 79 (64); HR EIMS m/z: found: 342.1465 $[M]^+$, $C_{20}H_{22}O_5$ requires: 342.1467; ^{13}C and ^{1}H NMR: Tables 1 and 2.

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