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Three New Diterpenoids from *Isodon Eriocalyx*

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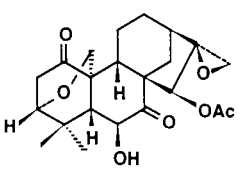
Abstract: Three new diterpenoids, eriocalyxins **C-E**, were isolated from *Isodon eriocalyx*. Their structures were elucidated as 6β-hydroxy-15β-acetoxy-3α, 20-epoxy-16β, 17-epoxy-*ent*-kaur-1,7-dione; 1α, 7β-dihydroxy-6β, 15β-diacetoxy-7, 20-epoxy-*ent*-kaur-16-ene; and 15β-acetoxy-1, 6-dioxo-6, 7-*seco*-*ent*-kaur-2, 16-dien-7, 20-olide by means of spectroscopic methods, including two-dimensional NMR techniques.

Keywords: *Isodon eriocalyx; Labiatae; ent*-kaurane diterpenoids; eriocalyxins C-E.



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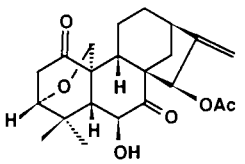

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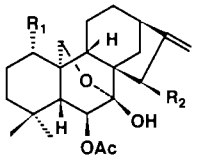
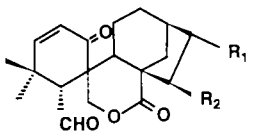


2. R_1 = OH, R_2 = OAc
5. R_1 = OAc, R_2 = OH



3. R_1 = =CH_2, R_2 = β-OAc
6. R_1 = α-CH_3, R_2 = =O

Isodon eriocalyx is known to be rich in *ent*-kaurenoids. In spite of that many *ent*-kaurenoids were isolated, new *ent*-kaurenoids were still isolated from collection in different regions[1-10]. From the dried leaves of this species collected in Heqing county, Yunnan, three new compounds, eriocalyxins C-E **1-3**, were isolated. In this paper, we report the structure elucidation of these new compounds by spectral analysis.

Eriocalyxin **C 1** $C_{22}H_{28}O_7$ (HRMS 404.1825 calc 404.1835), EIMS (70eV) m/z (rel. Int %): 404[M]$^+$ (10), 386[M-H_2O]$^+$ (10), 368[M-2H_2O]$^+$ (20), 344 (100), 326 (50), 288 (25), 245 (28), 231 (50), 213 (63); mp 191.5-192.5°. Its mass spectrum showed that the molecular ion (*m/z* 404) was 16 amu more than that of maoecrystal A **4**[2,3]. The ^{1}H, ^{13}C and DEPT spectra of **1** were very similar to those of **4** and the only difference was that instead of *exo*-methylene carbons in **4**, **1** had one quaternary carbon (δ67.8) and one methylene carbon (δ47.5) linked to oxygen. Thus, the structure of **1** should have the same skeleton type as that of **4**. Inspection of the ^{1}H-^{13}C COSY and COLOC spectra of **1**, indicated that the methylene signals at 2.92 ppm and 2.83 ppm (^{13}C chemical shift δ 47.5) correlated with quaternary carbon signal at δ 67.8, while the latter revealed the cross-peaks with a methylene signal at 1.95 ppm (H-14α) and two methine signals at 1.88 ppm (H-13) and 6.69 ppm (H-15). Thus, the quanternary carbon and methylene should be assigned to C-16 and C-17, respectively. **1** had a C-16, C-17 epoxy group instead of *exo*-methylene as in **4**. Comparison the ^{13}C NMR data of **1** with those of **4**, the chemical shift of C-9 (δ 39.7 ppm) in **1** was almost the same (δ 40.3 ppm)as that in **4**. The chemical shift of C-12 changed from 32.9 ppm in **4** to 28.7 ppm in **1**. Thus, the relative configuration of C-15-OAc should be same as in **4**. The relative configuration of epoxy-ring (C-16 and C-17) should be β-orientation[10]. Therefore, **1** should be 6β-hydroxy-15β-acetoxy-3α,20-epoxy-16β, 17-epoxy-*ent*-kaur-1,7-dione.

Eriocalyxin **D 2** $C_{24}H_{34}O_7$, HRMS 434.2328, calc 434.2305, EIMS (70eV) m/z (rel. Int %): 434[M]$^+$ (35), 392 (100), 332 (55), 314 (30), 227 (60); mp 208-210°. Its mass spectrum showed the same molecular ion as that of maoecrystal F **5**[4]. The ^{1}H, ^{13}C and DEPT spectra of **2** were very similar to those of **5** and the only difference between **5** and **2** was that the signals at δ 4.93 (1H, *dd*, *J* = 10.0, 4.0 Hz, H-1β) and δ 74.50 (C-1) in **5** were shifted upfield to δ 3.76 (1H, *dd*, *J* = 10.9, 5.2 Hz, H-1β) and δ 73.27 (C-1) in **2**, while the signal at δ 4.99 (1H, *t*, *J* = 2.5 Hz, H-15α) in **5** was shifted down field to δ 6.21 (1H, *brs*, H-15α) in **2**. These evidences indicated that a hydroxyl group should be assigned to C-1 and an acetyl group assigned to C-15 in **2**. Inspection of the ^{1}H-^{13}C COSY and COLOC spectra of **2**, exhibited cross peaks between H-6 (δ 5.01) with an acetyl group (δ 171.3) and H-15 (δ 6.21) with another acetyl group (δ 171.1), respectively. This information also confirmed the above deduction. The relative configuration of C-15-OAc should be same as in **5**. Therefore, **2** was deduced as 1α, 7β-dihydroxy-6β,15β-diacetoxy-7,20-epoxy-*ent*-kaur-16-ene.

Eriocalyxin **E 3** $C_{22}H_{26}O_6$, HRMS 386.1734, calc 386.1729, EIMS (70eV) m/z (rel. Int%): 386[M]$^+$ (10), 344 (5), 326 (8), 316 (80), 298 (60), 287 (40), 269 (15), 257 (40), 135 (100); mp 178-179.5°. Its mass spectrum showed that the molecular ion (m/z 386) was 42 amu more than that of eriocalyxin A **6**[3]. The ^{1}H, ^{13}C and DEPT spectra of **3** were very similar to those of **6** except for the D-ring. Instead of the methyl and carbonyl signals in **6**, signals for an *exo*-methylene and oxygen bearing methine carbons were observed in **3**. Analysis of the COSY and COLOC spectra of **3** revealed that the methine signal at δ5.57 ppm (δ 81.6, C-15) correlated with the quaternary carbon (δ 153.9), while the latter exhibited correlation with two methylene signals at δ 2.07 and 2.31 ppm (^{13}C δ 32.1 and 31.1, C-12 and C-14, respectively). Thus, **3** possessed an acetoxy group attached to C-15 instead of a carbonyl and an *exo*-methylene instead of a methyl group at

C-16, respectively. Because the chemical shift of C-9 changed from 42.6 ppm in **6** to 37.2 ppm in **1**, C-15-OAc should be at β-orientation on the basis of the γ-effect. Therefore, **3** was determined as 15β-acetoxy-1,6-dioxo-6,7-*seco-ent*-kaur-2,16-dien-7,20-olide.

Eriocalyxin **C** ^{1}H NMR (pyridine-d_5) δ: 6.69 (1, *brs*, H-15α), 5.02 (1H, *d*, *J* =11.8 Hz, H-6α), 4.86 (1H, *d*, *J* = 9.4 Hz, H-20a), 4.17 (1H, *d*, *J* = 9.4 Hz, H-20b), 3.77 (1H, *dd*, *J* = 3.4, 1.8 Hz, H-3β), 2.92 (1H, *d*, *J* = 4.5 Hz, H-17a), 2.83 (3H, overlapped, H_2-2 and H-17b), 1.95 (3H, *s*, OAc), 1.95 (1H, overlapped, H-14α), 1.88 (2H, overlapped, H-5β and H-13α), 1.71 (3H, *s*, Me-19), 1.23 (3H, *s*, Me-18). ^{13}C data shown in **Table 1**.

Eriocalyxin **D** ^{1}H NMR (pyridine-d_5) δ: 6.21 (1H, *brs*, H-15α), 5.83 (1H, *d*, *J* = 7.8 Hz, H-6α), 5.24 (1H, *brs*, H-17a), 5.11 (1H, *brs*, H-17b), 4.83 (1H, *d*, *J* = 9.6 Hz, H-20a), 4.38 (1H, *d*, *J* = 9.6 Hz, H-20b), 3.76 (1H, *dd*, *J* = 10.9, 5.2 Hz, H-1β), 2.56 (1H, *m*, H-13α), 2.29, 2.12 (each 3H, *s*, 2×OAc), 1.90 (1H, *d*, *J* = 7.8 Hz, H-5β), 1.19 (3H, *s*, Me-18), 0.93 (3H, *s*, Me-19). ^{13}C data shown in **Table 1**.

Eriocalyxin **E** ^{1}H NMR ($CDCl_3$) δ: 9.94 (1, *d*, *J* = 2.8 Hz, H-6), 6.53 (1H, *d*, *J* = 10.2 Hz, H-2), 5.88 (1H, *d*, *J* = 10.2 Hz, H-3), 5.57 (1H, *brs*, H-15α), 5.09 (1H, *brs*, H-17a), 4.90 (1H, *brs*, H-17b), 4.86 (1H, *d*, *J* = 11.0 Hz, H-20a), 4.60 (1H, *d*, *J* = 11.0 Hz, H-20b), 3.18 (1H, *d*, *J* = 2.8 Hz, H-5β), 2.71 (1H, *brs*, H-13α), 2.20 (3H, *s*, OAc), 1.35 (3H, *s*, Me-18), 1.23 (3H, *s*, Me-19). ^{13}C data shown in **Table 1**.

Table 1 ^{13}C NMR data of eriocalyxins C-E in pyridine-d_5

Carbon	1	2	3[a]
1	209.7 (*s*)	73.3 (*d*)	197.6 (*s*)
2	42.2 (*t*)	30.4 (*t*)	156.5 (*d*)
3	77.5 (*t*)	39.5 (*t*)	125.5 (*d*)
4	38.1 (*s*)	33.9 (*s*)	36.0 (*s*)
5	51.6 (*d*)*	55.7 (*d*)	57.9 (*d*)
6	71.9 (*d*)	75.6 (*d*)	200.1 (*d*)
7	208.9 (*s*)	95.4 (*s*)	172.5 (*s*)
8	58.1 (*s*)	52.1 (*s*)	50.9 (*s*)
9	39.7 (*d*)	46.5 (*d*)	37.2 (*d*)
10	51.8 (*s*)*	41.6 (*s*)	49.9 (*s*)
11	22.2 (*t*)	19.3 (*t*)	16.9 (*t*)
12	28.7 (*t*)	32.2 (*t*)	32.1 (*t*)*
13	34.9 (*d*)	37.1 (*d*)	36.3 (*d*)
14	35.7 (*t*)	27.4 (*t*)	31.5 (*t*)*
15	75.5 (*d*)	75.4 (*d*)	81.6 (*d*)
16	67.8 (*s*)	169.1 (*s*)	153.9 (*s*)
17	47.5 (*t*)	108.6 (*t*)	110.5 (*t*)
18	29.5 (*q*)	32.7 (*q*)	31.5 (*q*)
19	23.1 (*q*)	22.3 (*q*)	24.6 (*q*)
20	62.5 (*t*)	63.9 (*t*)	67.8 (*t*)
OAc	169.3	171.3	169.7
	20.4	171.1	20.9
		21.98	
		21.40	

a: The data was recorded in the $CDCl_3$.* Assignment may be exchangeable.

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