

Three New 6,7-Seco-Ent-Kaurane Diterpenoids from *Isodon eriocalyx*

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ABSTRACT - From the dried leaves of *I. eriocalyx*, three new 6,7-seco- *ent*-kaurane diterpenoids *epi*-eriocalyxin A (2), maoecrystal N (3) and maoecrystal O (4) were isolated. Meanwhile, the structure of a known constituent eriocalyxin A was revised.

Plants belonging to the *Isodon* genus are known to be rich in *ent*-kaurane diterpenoids, a number of which possess various biological activities such as cytotoxic^[1], antitumor^[2] and antibacterial^[3] activities.

As part of our search for biologically active constituents of this genus, the present paper deals with the isolation and identification of three new 6,7-seco-*ent*-kaurane diterpenoids named *epi*-eriocalyxin A (2), maoecrystal N (3) and maoecrystal O (4) from *Isodon eriocalyx* (Dunn) Hara. Additionally, two known compounds eriocalyxin A (1)^[4] and maoecrystal L (5)^[5] were also obtained.

Compound 1, C₂₀H₂₄O₅, was obtained as colorless crystals (from MeOH), mp: 242.0-244.0 °C. The spectral data of ¹H, ¹³C NMR, MS, IR, and UV were identical with those of eriocalyxin A reported previously^[4]. But the careful investigation of the ¹³C NMR data of 1 reminded us to reconsider the orientation of Me-16.

For *ent*-kaurane diterpenoids, the chemical shifts of C-12, 14 and 17 were typical for differentiating the orientation of Me-16^[5,6]. The upfield shift of C-14 at about δ 29 ppm was characterized for Me-16 α while the upfield shift of C-12 at about δ 18 ppm for Me-16 β due to γ - steric compression effect. Meanwhile, the chemical shift of C-17 was also useful for distinguishing the stereochemistry of Me-16. When the Me-16 was β -orientation, the chemical shift of C-17 was δ 11 ppm or so, otherwise, the δ value was about δ 17 ppm because of the space effect mentioned above^[5].

The chemical shift of C-14 in **1** shifted to upfield at δ 30.0 ppm and the δ value of C-17 was 16.7 ppm. Consequently, the orientation of Me-16 in **1** should be revised as α . The revised structure of eriocalyxin A was 16(S)-methyl-1,6,15-trioxo-6,7-*seco-ent*-kaur-2-en-7,20-olide.

Epi-ericalyxin A (**2**) was obtained as a mixture which gave only one spot on TLC. The molecular formula $C_{20}H_{24}O_5$ was analyzed from EIMS (mol. ion peak at m/z 344 $[M]^+$). The IR, UV and NMR spectra clearly showed that the mixture was composed of two quite similar *ent*-kaurane diterpenoids eriocalyxin A (**1**) and **2**. The comparison of 1H and ^{13}C NMR signals of **2** with those of **1** indicated that **2** and **1** were epimeric at C-16. The β -orientation of Me-16 in **2** was confirmed by the upfield shift of C-12 at δ 17.6 ppm and C-17 at δ 11.4 ppm owing to the γ -steric compression effect between Me-16 β and H-12 β each other^[6]. Thus, compound **2** was identified as 16(R)-methyl-1,6,15-trioxo-6,7-*seco-ent*-kaur-2-en-7,20-olide.

Maoecrystal N (**3**), mp: 290.0-292.0°C, $[\alpha]_D^{25} = +167.83^\circ$ ($c = 0.36$, C_5D_5N) was shown to have a molecular formula of $C_{20}H_{24}O_6$ by HR EIMS (360.1532 $[M]^+$, calc. 360.1573). The analysis of 1H and ^{13}C NMR data revealed that **3** resembled closely eriocalyxin A (**1**) except for ring A. The carbon signal at δ 201.7 ppm assigned to -CHO group in **1** was replaced by that at δ 172.4 ppm arising from -COOH group. The proton signal at δ 10.08 ppm corresponding to -CHO group' also disappeared in **3**. All these facts showed the presence of -COOH instead of -CHO group in **3**.

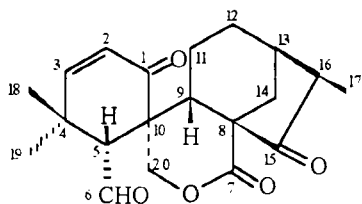
The results obtained from IR spectral data further confirmed the conclusion. The two absorption at 2860 and 2740 cm^{-1} owing to Fermi resonance of -CHO group was absent in **3** whereas a strong absorption at about 3000 cm^{-1} (br.) typical for hydroxyl of carboxy group was noticed.

Therefore, compound **3** was identified as 16(S)-methyl-6 α -carboxy-1,15-dioxo-6, 7-*seco-ent*-kaur-2-en-7,20-olide.

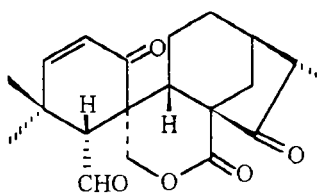
Maoecrystal O (**4**) was yielded as colorless crystals (from MeOH), mp: 268.5-270.0°C, $[\alpha]_D^{25} = -3.66^\circ$ ($c=0.41$, $CHCl_3$). Its 1H and ^{13}C NMR spectral data were quite similar to those of maoecrystal L (**5**). The only difference between **4** and **5** was that the carbon signal at δ 203.8 ppm arising from -CHO group in **5** was replaced by that at δ 173.9 ppm from -COOH group. Meanwhile, the proton signal at δ 9.98 ppm corresponding to -CHO in **5** was absent in **4**.

This assignment was confirmed by the molecular ion peak at m/z 406 in EI mass spectra corresponding to $C_{22}H_{30}O_7$. The two absorption at 2850 and 2720 cm^{-1} characterized for the existence of -CHO group in **5** disappeared in **4** and there was a strong absorption at 3260 cm^{-1} owing to -COOH group being observed in the IR spectra.

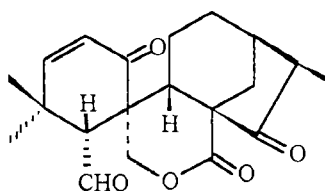
Accordingly, the structure of **4** was identified as 16(S)-1 α -acetoxy-6 α -carboxy-15-oxo-6,7-*seco-ent*-kauran-7,20-olide.



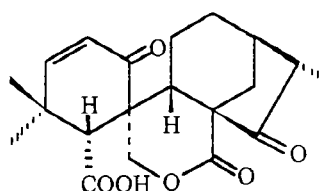
Eriocalyxin A
(reported previously)



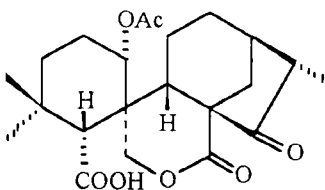
1



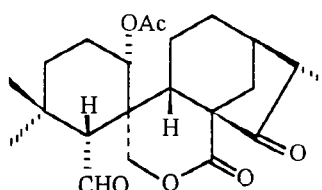
2



3



4



5

Table 1 ^{13}C NMR data of 1 - 4 in $\text{C}_5\text{D}_5\text{N}$
(100 MHz, δ in ppm with reference to the signal of $\text{C}_5\text{D}_5\text{N}$)

Carbon	1	2	3*	4
1	198.1 s	198.0 s	198.2 s	75.8 s
2	125.0 d	125.1 d	124.6 d	24.7 d
3	157.5 d	157.5 d	157.2 d	39.5 d
4	36.2 s	36.2 s	35.9 s	34.0 s
5	57.5 d	57.6 d	54.3 d	58.6 d
6	201.7 d	201.7 d	172.4 s	173.9 s
7	169.6 s	169.7 s	169.6 s	170.2 s
8	59.9 s	59.2 s	59.1 s	59.4 s
9	42.6 d	42.8 d	43.1 d	45.2 d
10	50.6 s	50.4 s	50.2 s	43.1 s
11	18.1 t	20.0 t	18.0 t	17.8 t
12	30.0 t	17.6 t	29.9 t	29.8 t
13	35.7 d	32.6 d	35.4 d	35.6 d
14	30.0 t	32.8 t	29.4	28.8 t
15	216.7 s	217.0 s	216.2t s	216.5 s
16	51.0 d	48.9 d	51.0 d	51.2 d
17	16.7 q	11.4 q	16.6 q	16.7 q
18	31.2 q	31.1 q	31.9 q	33.5 q
19	24.0 q	24.1 q	24.7 q	23.3 q
20	69.3 t	69.5 t	69.3 t	68.8 t
OAc				170.2
				21.4

* The data were measured in CDCl_3 with reference to the signal of CDCl_3

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