

毛萼香茶菜中的三个新的对映-贝壳杉烷型二萜

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摘要 从采自云南省江川县的毛萼香茶菜 (*Isodon eriocalyx*) 的甲醇提取物中分离得到 3 个新的 6, 7-螺断-对映-贝壳杉烷型二萜: 表毛萼甲素, 毛萼晶 N 和毛萼晶 O; 同时还分离到 2 个已知化合物: 毛萼甲素及毛萼晶 L, 并修正了毛萼甲素的结构。

关键词 唇形科, 毛萼香茶菜, 二萜

THREE NEW 6,7-SECO-ENT-KAURANE DITERPENOIDS FROM ISODON ERIOCALYX

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Abstract Three new 6,7-seco-ent-kaurane diterpenoids named *epi-eriocalyxin A* (2), maoecrystal N (3) and maoecrystal O (4) together with two known constituents *eriocalyxin A* (1) and maoecrystal L (5) were isolated from the dried leaves of *Isodon eriocalyx*. Meanwhile, the structure of *eriocalyxin A* was revised.

Key words Labiatae, *Isodon eriocalyx*, Diterpenoids

Isodon eriocalyx (Dunn.) Hara, a perennial herb or shrub of Labiatae family, is widely distributed in Southwest China. It has long been used as folk medicine to cure sore throat, inflammation and interdigital disease (吴征镒等, 1977). A series of new *ent-kaurane* diterpenoids have been isolated from the dried leaves of *I. eriocalyx* collected in five different regions of Yunnan Province, China (Hassan *et al*, 1994; Takeda *et al*, 1995).

Further investigation on the same plant led to the isolation and determination of three new 6, 7- *seco-ent-kaurane* diterpenoids named *epi-eriocalyxin A* (2), maoecrystal N (3) and maoecrystal O (4) as well as two known constituents *eriocalyxin A* (1) (王宗玉等, 1982) and maoecrystal L (5) (Shen *et al*, 1994).

RESULTS AND DISCUSSION

Compound 1, $C_{20}H_{24}O_5$, was obtained as colorless crystals (from MeOH). The spectral data of 1H , ^{13}C NMR, MS, IR, and UV were identical with those of *eriocalyxin A* reported previously. The

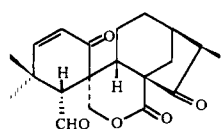
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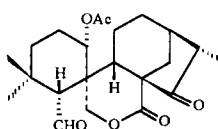
stereochemistry of Me-16 in ericalyxin A was established as β -orientation, but there was no direct evidence to confirm the determination because of technical limits at that time. Comparison [Table 1] of the ^{13}C NMR data of 1 with those of maocrystal L and laxiflorin C (Sun *et al*, 1995), both of which possessed the same skeleton as 1, reminded us to reconsider the orientation of Me-16.

The stereochemistry of Me-16 in laxiflorin C was confirmed as β -orientation by the NOE effects between H-12 β and C-16 methyl, and the unique upfield shift of C-12 (δ 17.9 owing to the γ -effect of Me-16 β). The α -orientation of Me-16 in maocrystal L was also supported by the significant NOEs between H-14 β and Me-16, and the upfield shift of C-14 (δ 28.4 due to the γ -effect of Me-16 α). Thus, the orientation of Me-16 could be determined by the upfield shift of C-14 or C-12. The upfield shift of C-14 at about δ 28.4 was characterized for Me-16 α while the upfield shift of C-12 at about δ 18 for Me-16 β . 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 or so. Otherwise, the δ value was about δ 17 because of the space effect mentioned above.

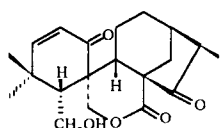
In conclusion, the chemical shifts of C-12, 14 and 17 were typical for differentiating the orientation of Me-16.



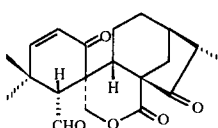
Eriocalyxin A
(reported previously)



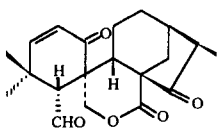
Maocrystal L (15)



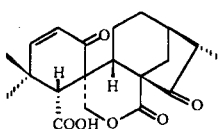
Laxiflorin C



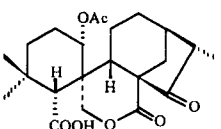
1



2



3



4

Maocrystal N (3) contained three methyls, four methylenes (including one oxygen-bearing methylene), four methines, three quaternary carbons, two olefinic carbons and four carbonyl carbons judging from its ^1H and ^{13}C NMR spectra. These facts, together with EI mass (ion at m/z 360 $[\text{M}]^+$) exhibited 3 having a molecular formula of $\text{C}_{20}\text{H}_{24}\text{O}_6$.

The analysis of ^1H and ^{13}C NMR data revealed that 3 resembled closely to ericalyxin A (1) except for

The chemical shifts of ring C and D in 1 were quite similar to those of maocrystal L. Consequently, the orientation of Me-16 in 1 should be revised as α . The revised structure of ericalyxin 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 IR, UV and NMR spectra clearly showed that the mixture was composed of two quite similar ent-kaurane diterpenoids in a 1:1 ratio, and one of them was easily determined as ericalyxin A (1). 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 and C-17 at δ 11.4 owing to the γ -steric compression effect between Me-16 β and H-12 β . Thus, compound 2 was identified as 16(R)-methyl-1,6,15-trioxo-6,7-seco-ent-kaur-2-en-7,20-olide.

A-ring. The carbon signal at δ 201.7 assigned to -CHO group in 1 was replaced by that at δ 172.4 arising from -COOH group. The proton signal at δ 10.08 corresponding to -CHO group in 1 was also disappeared in 3. All these facts showed the presence of -COOH in 3 instead of -CHO group in 1.

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 in 1 was absent in 3, whereas a strong absorption at about 3000 cm^{-1} (br.) typical for hydroxyl of carboxyl group was noticed in 3. 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). 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 arising from -CHO group in 5 was replaced by that at δ 173.9 from -COOH group in 4. Meanwhile, the proton signal at δ 9.98 corresponding to -CHO in 5 was absent in 4. The replacement of -CHO by -COOH group in 4 resulted in upfield shift of C-5 by 3.0 ppm.

This assignment was confirmed by the molecular ion peak at m/z 406 in EI mass spectra corresponding to $\text{C}_{22}\text{H}_{30}\text{O}_7$. The two absorption at 2850 and 2720 cm^{-1} characterized for the existence of -CHO group in 5 was disappeared in 4 and there was a strong absorption at 3260 cm^{-1} owing to -COOH group being observed of the IR spectra in 4.

Table 1 ^{13}C NMR data of maoecrystal L, eriocalyxin A*, laxiflorin C, and 1~4 in $\text{C}_5\text{D}_5\text{N}$ (400 MHz, δ with reference to the signal of $\text{C}_5\text{D}_5\text{N}$)

Carbon	Maoecrystal L (5)	Eriocalyxin A*	1	Laxiflorin C	2	3 [#]	4
1	75.3	197.3	198.1	201.0	198.0	198.2	75.8
2	24.3	125.1	125.0	124.5	125.1	124.6	24.7
3	39.8	156.6	157.5	158.9	157.5	157.2	39.5
4	34.1	36.2	36.2	36.7	36.2	35.9	34.0
5	61.6	57.5	57.5	47.4	57.6	54.3	58.6
6	203.8	200.1	201.7	58.2	201.7	172.4	173.9
7	170.0	169.1	169.6	175.5	169.7	169.6	170.2
8	59.3	59.8	59.9	59.5	59.2	59.1	59.4
9	43.6	42.6	42.6	41.8	42.8	43.1	45.2
10	43.7	50.0	50.6	52.3	50.4	50.2	43.1
11	17.5	17.8	18.1	20.2	20.0	18.0	17.8
12	29.4	29.7	30.0	17.9	17.6	29.9	29.8
13	35.5	35.4	35.7	32.6	32.6	35.4	35.6
14	28.8	29.5	30.0	32.7	32.8	29.4	28.8
15	216.1	216.2	216.7	217.5	217.0	216.2	216.5
16	50.9	51.1	51.0	48.8	48.9	51.0	51.2
17	16.0	16.8	16.7	11.8	11.4	16.6	16.7
18	32.6	31.5	31.2	31.7	31.1	31.9	33.5
19	23.8	24.3	24.0	23.8	24.1	24.7	23.3
20	68.0	68.7	69.3	70.8	69.5	69.3	68.8
OAc	170.0						170.2
	21.3						

* The data of eriocalyxin A reported by Wang et al., 1982

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

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

EXPRIMENTAL

Mps: uncorr.. Optical rotations were taken on a JASCO-20C digital polarimeter. IR spectra were recorded with a Perkin-Elmer 577 spectrometer. UV spectra were obtained on a UV-210A spectrometer. MS spectra were measured on a VG Autospec spectrometer. NMR spectra were run on a Bruker AM-400 spectrometer. The chemical shifts (δ) were expressed in ppm with reference to the solvent signals. Coupling constants (J) were given in Hz.

Plant Material *Isodon eriocalyx* (Dunn.) Hara was collected in Jiangchuan Prefecture, Yunnan Province, China, in September 10, 1994, and identified by Prof. H. W. Li. A voucher specimen was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, P. R. China.

Extraction and Isolation Dried powdered leaves of *I. eriocalyx* (Dunn.) Hara (11.9 kg) were extracted with MeOH (4 \times 401) under reflux and then concentrated in vacuum to give crude extract (978 g). The extract was suspended in H₂O and then successively fractionated with petroleum ether (60~90°C) and AcOEt. The AcOEt extract (395 g) was chromatographed on a silica gel column (1.6 kg, 200~300 mesh) eluting with CHCl₃ by increasing amount of Me₂CO to yield seven fractions. Fraction I, II and III were submitted to MCI gel to decolor green pigments. Then each fraction was subjected to silica gel column chromatography repeatedly followed by crystallization and finally afforded compounds: 1(3.1 g), 2(110 mg), 3(120 mg), 4(210 mg) and 5 (70 mg).

Eriocalyxin A (1), C₂₀H₂₄O₅, colorless crystals (MeOH), mp: 242~244°C; IR ν_{\max}^{KBr} cm⁻¹: 2956, 2860, 2740, 1736, 1721, 1705, 1664, 1300, 1211, 1089, 1060, 1045, 912 and 831; UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 228.5 (4.03); EIMS (70 eV) m/z (%): 344[M]⁺(6), 316[M-CO]⁺(98), 301 (13), 287 (46), 269 (21), 257 (40), 227 (32), 165 (21), 1498 (43), 135 (100), 105 (41), 79 (65), 67 (46), and 55 (64); ¹H NMR (pyridine-d₅) δ : 5.94 (1H, d, J=10.0 Hz, H-2), 6.51 (1H, d, J=10.0 Hz, H-3), 10.08 (1H, d, J=3.2 Hz, H-6), 1.05 (3H, d, J=7.6 Hz, CH₃-16 α), 1.27 (3H, s, CH₃-18), 1.16 (3H, s, CH₃-19), 4.98 (1H, d, J=11.2 Hz, H-20b) and 5.31 (1H, d, J=11.2 Hz, H-20a); ¹³C NMR data see table 1.

Epi-eriocalyxin A (2), C₂₀H₂₄O₅, colorless crystals (MeOH); IR ν_{\max}^{KBr} cm⁻¹: 2910, 2840, 2740, 1730, 1703, 1660, 1450, 1360, 1245, 1208, 1085, 1040 and 910; UV $\lambda_{\max}^{\text{MeOH}}$ nm: 228.5; EIMS (70 eV) m/z (%): 344 [M]⁺(4), 316 [M-CO]⁺(69), 301 (7), 287 (35), 269 (12), 257 (31), 277 (24), 164 (24), 135 (100), 107 (61), 91 (59), 79 (91), 67 (71) and 55(97); ¹H NMR (pyridine-d₅) δ : 5.94(1H, d, J=10.0 Hz, H-2), 6.5(1H,d, J-10.0 Hz, H-3), 10.06(1H, d, J=3.6 Hz, H-6), 1.00(1H, d, J=7.2 Hz, CH₃-16 β), 1.27(3H, s, CH₃-18), 1.16(3H, s, CH₃-19), 4.97(1H, d, J=11.2 Hz, H-20b) and 5.32(1H, d, J=11.2 Hz, H-20a); ¹³C NMR data see Table 1.

Maoecrystal N (3), C₂₀H₂₄O₆, Colorless crystals (MeOH), mp: 290~292°C, [α]_D²⁵+167.8° (C₅H₅N; c 0.359); IR ν_{\max}^{KBr} cm⁻¹: 3000 (br), 1750, 1740, 1700, 1400, 1310, 1270, 1240, 1212, 1160, 1110, 1060, and 930; UV $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 228.0 (3.93); EIMS (70 eV) m/z (%): 360 [M]⁺(3), 332 [M-CO]⁺(100), 301 (54), 79 (66), 67 (44) and 55 (75); HR FABMS (positive ion mode) m/z (%): 360.1532 (calc. 360.1573); ¹H NMR (CDCl₃) δ : 5.80(1H, d, J=10.2 Hz, H-2), 6.56(1H, d, J=10.2 Hz, H-3), 1.09(3H, d, J=7.6 Hz, CH₃-16 α), 1.29(3H, s, CH₃-18), 1.27(3H, s, CH₃-19), 4.67(1H, d, J=11.5 Hz, H-20b) and 5.11(1H, d, J=11.5 Hz,

H-20a); ^{13}C NMR data see Table 1.

Maoecrystal O (4), $\text{C}_{22}\text{H}_{30}\text{O}_7$, colorless crystals (MeOH), mp: 268~270 $^{\circ}\text{C}$, $[\alpha]_{\text{D}}^{25}$ -3.7 $^{\circ}$ (CHCl_3 ; c 0.410); IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3260, 2940, 1760, 1728, 1686, 1360, 1223, 1072, 1032 and 910; EIMS (70 eV) m/z (%): 406 $[\text{M}]^+$ (3), 378 $[\text{M}-\text{CO}]^+$ (100), 362 (5), 349 (41), 318 (38), 290 (40), 272 (38), 164 (44), 149 (54), 135 (42), 120 (56), 105 (73), 83 (91), 67 (56) and 55 (87); HR FABMS (positive ion mode) m/z: 406.1992 (calc. 406.2028); ^1H NMR(pyridine- d_5) δ : 5.13(1H, d, J=3.3, 11.5 Hz, H-1 β), 0.98(3H, d, J=7.0 Hz, CH_3 -16 α), 1.24(3H, s, CH_3 -18), 1.08(3H, s, CH_3 -19), 5.39(1H, d, J=12.7 Hz, H-20b), 5.46(1H, d, J=12.7 Hz, H-20a) and 2.18(3H, s, OAc); ^{13}C NMR data see Table 1.

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