Novel *ent*-Abietane Diterpenoids from *Isodon eriocalyx* var. *laxiflora*

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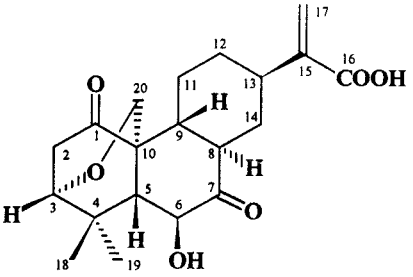
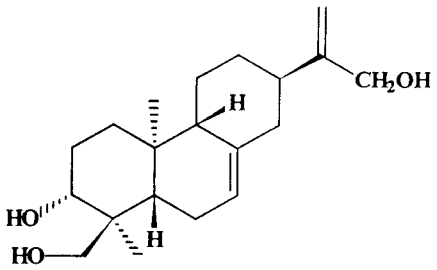
Two novel *ent*-abietane diterpenoids, 3α,20-epoxy-6β-hydroxy-1,7-dioxo-*ent*-abiet-15(17)-en-16-oic acid (**1**) and *ent*-abieta-7,15(17)-diene-3β,16,18-triol (**2**) were isolated from *Isodon eriocalyx* var. *laxiflora*. Their structures were determined by extensive spectroscopic analysis and confirmed by X-ray crystallography. Compound **1** is an unprecedented example that establishes that a naturally occurring *ent*-abietane diterpenoid can have an oxygenation pattern almost identical to those of 3α,20-epoxy-*ent*-kaurane diterpenoids.

1. Introduction. – *Isodon eriocalyx* (DUNN) HARA var. *laxiflora* C. Y. WU et H. W. LI (Labietae), a perennial shrub, is distributed in Yunnan province, P. R. China. It belongs to the genus *Isodon*, which are natural drug resources having antitumor, antibacterial, and anti-inflammatory activities, and are known for being rich in *ent*-kaurane diterpenoids [1][2]. *I. eriocalyx* has long been used as a traditional plant medicine for sore throat, inflammation, and interdigitali as well as for reducing blood pressure [3]. The entirety of the diterpenoids extracted from *I. eriocalyx* has been made into a drug for throat disease named 'yanshukang' in China in 1996 [1]. Until now, about 40 *ent*-kaurane diterpenoids have been reported from *I. eriocalyx* and its variant [4–10]. Our previous work on the leaves of *Isodon eriocalyx* var. *laxiflora* for bioactive constituents have yielded two novel 3,6-epoxy-6,7:8,15-seco-*ent*-kaurane-7,20-olide diterpenoids [11]. The continuous investigation and careful examination of this material led to the discovery of two additional novel *ent*-abietane diterpenoids **1** and **2** (*Fig. 1*). In the following, we describe the isolation and structure elucidation of these two compounds.

2. Results and Discussion. – Compound **1** (*Fig. 1*), obtained as colorless lumpish crystals from Me_2CO, gave a molecular-ion peak at *m*/*z* 362 in the EI-MS, consistent with a molecular formula $C_{20}H_{26}O_6$ by its high-resolution EI-MS. The IR spectrum indicated the presence of OH groups (3374, 3107 cm^{-1}), a carboxylic acid (1700 cm^{-1}), carbonyl groups (1700 cm^{-1}), and a C=C bond (3005, 1631 cm^{-1}). Considering the constituents isolated so far from *I. eriocalyx* and its variant, compound **1** was originally presumed to be a 3α,20-epoxy-*ent*-kauranoid by its ^{1}H- and ^{13}C-NMR spectra (*Tables 1* and *2*). However, the skeletons of *ent*-kaurane diterpenoids usually possess three characteristic methines (C(5), C(9), and C(13)) and three quaternary C-atoms (C(4), C(8), and C(10)). Unlike normal *ent*-kauranoids, compound **1** contains two quaternary



1



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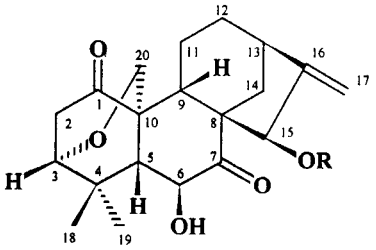


3 R = Ac

4 R = H

Fig. 1. *Structures of compounds* **1**–**4**

C-atoms and four methines as established by detailed analysis of its ^{13}C-NMR and DEPT spectra, which correspond much more likely to the skeleton of an abietane-type diterpenoid. Comparison of compound **1** with maoecrystal A (**3**) [8], which, as the major *ent*-kaurane diterpenoid, was also obtained in this experiment, revealed that the two compounds **1** and **2** were very similar to **3**, having the same ring A and almost identical oxygenation substituents at rings B and C. Compound **1** differed from **3** mainly by a lack of linkage between C(8) and C(15) (in **3**) or C(16) (in **1**). A plausible biosynthetic origin for the skeleton of **1** can be proposed, *i.e.*, the C-skeleton of **1** is probably derived biogenetically from **3** as the result of the cleavage of ring D (see *Scheme*), which is, in a way, similar to the previously proposed biogenic pathway for laxiflorins F and G [11]. On the other hand, it is noteworthy that H–C(8) of compound **1** is in a position exactly opposite compared with that of laxiflorins F and G with respect to the projection plane of the C-skeleton. Considering the co-occurrence of H–C(8) of **1** in the α-position and the close resemblance of its O-pattern to that of *ent*-kauranoids, but compatible with the structural features of the hitherto only synthetic *ent*-abietane diterpenoid, a seco-aldehyde transformed from shikokianidin by an acid treatment [12], we propose an *ent*-abietane diterpenoid structure for compound **1**. 2D-NMR Experiments (including ^{1}H,^{1}H COSY, HMQC, HMBC (*Fig. 2*) and ROESY (*Fig. 3*)) and X-ray crystallographic diffraction (*Fig. 4*) indeed established the structure of **1** as 3α,20-epoxy-6β-hydroxy-1,7-dioxo-*ent*-abiet-15(17)-en-16-oic acid, which we name laxiflorin N.

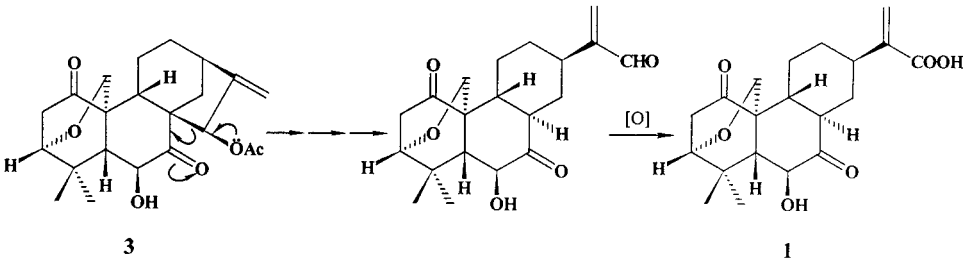
Table 1. *^{1}H-NMR Data* (500 MHz) *of Compounds* **1** *and* **2** *in (D$_5$)Pyridine.* δ in ppm, J in Hz.

1		**2**	
H–C(1)	–	H_a–C(1)	1.80 (br. *d*, J = 13.1, 1 H)
		H_b–C(1)	1.25 (overlap, 1 H)
H–C(2)	2.75 (br. *s*, 2 H)	H–C(2)	2.02 (overlap, 1 H)
			1.96 (overlap, 1 H)
H_β–C(3)	3.75 (br. *s*, 1 H)	H_β–C(3)	4.24 (*t*, J = 8.0, 1 H)
H_β–C(5)	1.83 (*d*, J = 11.3, 1 H)	H_β–C(5)	1.92 (overlap, 1 H)
H_α–C(6)	4.77 (*d*, J = 11.3, 1 H)	CH_2(6)	2.00 (overlap, 1 H)
			1.91 (overlap, 1 H)
H–C(7)	–	H–C(7)	5.35 (br. *s*, 1 H)
H_α–C(8)	2.45 (br. *t*, J = 12.5, 1 H)	H–C(8)	–
H_β–C(9)	2.24 (br. *t*, J = 12.5, 1 H)	H_β–C(9)	1.69 (overlap, 1 H)
H_α–C(11)	1.05 (overlap, 1 H)	H_a–C(11)	1.70 (overlap, 1 H)
H_β–C(11)	1.95 (br. *d*, J = 12.5, 1 H)	H_b–C(11)	1.18 (br. *d*, J = 13.0, 1 H)
H_α–C(12)	1.89 (br. *d*, J = 12.5, 1 H)	H_a–C(12)	1.93 (overlap, 1 H)
H_β–C(12)	1.24 (*qd*, J = 12.5, 1.2, 1 H)	H_b–C(12)	1.28 (overlap, 1 H)
H_α–C(13)	2.74 (overlap, 1 H)	H_α–C(13)	2.05 (overlap, 1 H)
H_α–C(14)	2.37 (br. *d*, J = 12.5, 1 H)	H_a–C(14)	2.48 (br. *d*, J = 12.0, 1 H)
H_β–C(14)	1.53 (*q*, J = 12.5, 1 H)	H_b–C(14)	2.08 (overlap, 1 H)
H–C(16)	–	H–C(16)	4.43 (*s*, 2 H)
H_a–C(17)	6.48 (*s*, 1 H)	H_a–C(17)	5.45 (*s*, 1 H)
H_b–C(17)	5.59 (*s*, 1 H)	H_b–C(17)	5.04 (*s*, 1 H)
Me(18)	1.11 (*s*, 3 H)	H_a–C(18)	4.12 (*d*, J = 10.5, 1 H)
		H_b–C(18)	3.66 (*d*, J = 10.5, 1 H)
Me(19)	1.64 (*s*, 3 H)	Me(19)	1.14 (*s*, 3 H)
H_a–C(20)	4.76 (*d*, J = 9.8, 1 H)	Me(20)	0.91 (*s*, 3 H)
H_b–C(20)	4.11 (*dd*, J = 9.8, 1.4, 1 H)		

Table 2. *^{13}C-NMR Data* (125 MHz) *of Compounds* **1** *and* **2** *in (D$_5$)Pyridine and of Its 15*-O-*Deacetyl Derivative* **4** *and Comparison with Those of Maoecrystal* (**3**). δ in ppm.

	1	**3**	**4**	**2**
C(1)	209.5 (*s*)	208.2 (*s*)	209.1 (*s*)	38.2 (*t*)
C(2)	42.0 (*t*)	41.7 (*t*)	42.2 (*t*)	27.9 (*t*)
C(3)	78.0 (*d*)	77.0 (*d*)	77.5 (*d*)	73.9 (*d*)
C(4)	38.3 (*s*)	37.6 (*s*)	38.1 (*s*)	43.4 (*s*)
C(5)	54.9 (*d*)	51.9 (*d*)	51.8 (*d*)	43.1 (*d*)
C(6)	74.2 (*d*)	71.0 (*d*)	72.1 (*d*)	23.5 (*t*)
C(7)	210.8 (*s*)	209.5 (*s*)	212.0 (*s*)	120.7 (*d*)
C(8)	46.2 (*d*)	55.8 (*s*)	57.2 (*s*)	137.4 (*s*)
C(9)	43.1 (*d*)	34.7 (*d*)	40.0 (*d*)	52.6 (*d*)
C(10)	50.2 (*s*)	51.4 (*s*)	52.0 (*s*)	35.4 (*s*)
C(11)	29.1 (*t*)	20.4 (*t*)	21.2 (*t*)	25.9 (*t*)
C(12)	32.0 (*t*)	32.5 (*t*)	33.3 (*t*)	32.2 (*t*)
C(13)	38.0 (*d*)	39.6 (*d*)	33.6 (*d*)	41.7 (*d*)
C(14)	32.3 (*t*)	35.8 (*t*)	36.3 (*t*)	41.5 (*t*)
C(15)	147.1 (*s*)	73.9 (*d*)	74.6 (*d*)	155.6 (*s*)
C(16)	169.6 (*s*)	149.8 (*s*)	156.5 (*s*)	64.6 (*t*)
C(17)	122.1 (*t*)	108.7 (*t*)	106.3 (*t*)	107.0 (*t*)
C(18)	29.5 (*q*)	29.2 (*q*)	29.5 (*q*)	68.0 (*t*)
C(19)	23.5 (*q*)	22.9 (*q*)	23.3 (*q*)	13.0 (*q*)
C(20)	60.3 (*t*)	62.0 (*t*)	62.6 (*t*)	15.9 (*q*)

Scheme 1. *Postulated Biogenesis of Compound* **1**



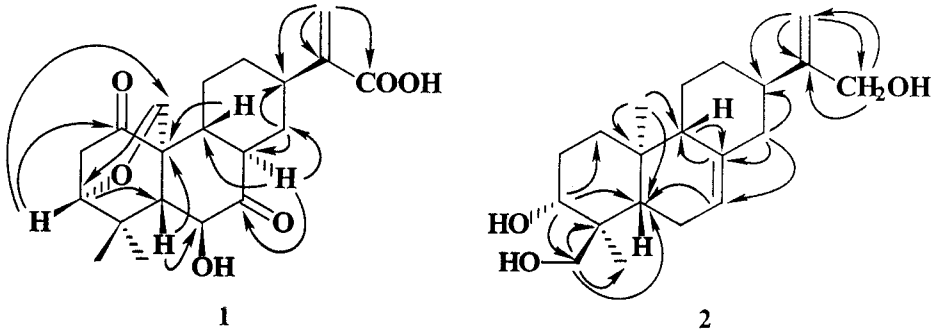


Fig. 2. *Key HMBC correlations of compounds* **1** *and* **2**

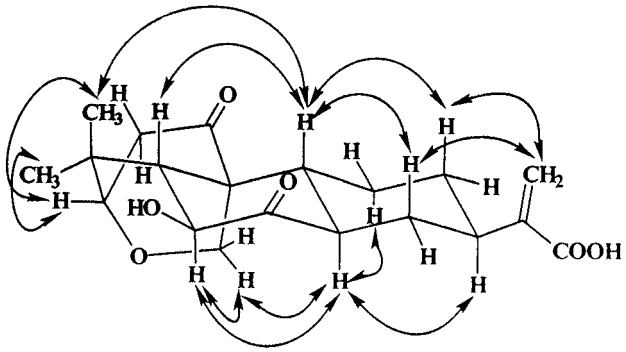


Fig. 3. *Key ROESY correlations of compound* **1**

The ^{1}H-NMR spectrum of **1** (*Table 1*) displayed signals at δ 1.11 (*s*, 3 H) and 1.64 (*s*, 3 H) for two tertiary Me groups, at δ 6.48 (*s*, 1 H) for 5.59 (*s*, 1 H) for two olefinic protons, and at δ 4.76 (*d*, $J = 9.8$ Hz, 1 H), 4.11 (*dd*, $J = 9.8$, 1.4 Hz, 1 H), 4.77 (*d*, $J = 11.3$ Hz, 1 H), and 3.75 (br. *s*, 1 H) for four protons attached to O-bearing C-atoms. In the low-field region of the ^{13}C-NMR spectrum (*Table 2*), the signals for an α,β-unsaturated carboxylic acid moiety were observed at δ 169.6 (*s*), 147.1 (*s*), and 122.1 (*t*), along with those of two isolated keto groups at δ 209.5 (*s*) and 210.8 (*s*). In the high-field region, the signals for two Me, five CH_2 (including 1 O–CH_2), six CH (including two O–CH), and two quaternary C-atoms were found. All spectral evidence obviously suggested the skeleton of a diterpenoid. On the basis of the previous reports that all diterpenoids isolated from *I. eriocalyx* were of the *ent*-kaurane type, coupled with the characteristic signals of the O–CH group (δ(C) 78.0 (*d*) and δ(H) 3.75 (br. *s*, 1 H), assignable to C(3) and H–C(3), resp.) and of the O–CH_2

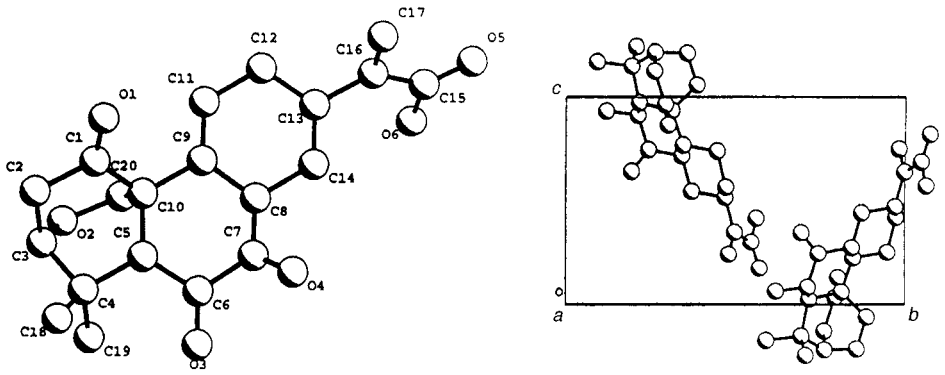


Fig. 4. *X-Ray crystallographic structure of compound* **1**

group (δ(C) 60.3 (*t*) and δ(H) 4.76 (*d*, $J = 9.8$ Hz, 1 H), and 4.11 (*dd*, $J = 9.8$, 1.4 Hz, 1 H), attributable to C(20) and 2 H–C(20), resp.), compound **1** was originally presumed to be a 3α,20-epoxy-*ent*-kaurane diterpenoid. The formation of an O-bridge between C(3) and C(20) was established by the ^{1}H,^{13}C long-range correlations of H–C(3)/C(20) and CH_2(20)/C(3) in the HMBC spectrum (*Fig. 2*). However, through a very careful comparison, we noticed that the ^{13}C-NMR data of **1** closely resembled those of maoecrystal A (**3**) (*Table 2*) [8]. Except for the signals of C(8), C(15)/C(16), and C(17), both compounds showed similar signals for rings A, B, and C. As the most outstanding difference between **1** and **3**, it was easily recognized that in the ^{13}C-NMR spectrum of **3**, the signal for the quaternary C(8) was replaced by a methine signal at δ 46.2 (*d*) in **1**. This change accounted for the disappearance of the linkage between C(8) and C(15)/C(16) that forms the five-membered ring D in normal *ent*-kauranoids and suggested an *ent*-abietane diterpenoid instead of an *ent*-kauranoid structure for compound **1**. The α,β-unsaturated carboxylic acid residue could be attributed to the C(15), C(17), and C(16) moiety on the ground of the HMBC interactions of the proton signals at δ 6.48 (*s*, 1 H) and 5.59 (*s*, 1 H) of CH_2(17) with the C-signals at δ 169.6 (*s*) and 38.0 (*d*) arising from C(16) and C(13), respectively. Based on extensive ^{1}H,^{1}H COSY, HMQC, and further HMBC analysis, other O-functionalities in **1** were established to remain unchanged comparing with those of **3**.

The relative configurations of **1** were deduced by ROESY experiments (*Fig. 3*). The NOE correlations of H_a–C(20) (δ 4.76 (*d*, $J = 9.8$ Hz, 1 H)) with H–C(6) (δ 4.77 (*d*, $J = 11.3$ Hz, 1 H)) and H–C(8) (δ 2.45 (br. *t*, $J = 12.5$ Hz, 1 H)), of H–C(6) with H–C(8), and of H–C(8) with H–C(13) (δ 2.74 (overlap, 1 H)) disclosed that H–C(6), H–C(8), and H–C(13) were α-oriented. H–C(5) (δ 1.83 (*d*, $J = 11.3$ Hz, 1 H)) was deduced to be β-positioned from the coupling constant J(H–C(5),H–C(6)) = 11.3 Hz and the ROESY correlation of H–C(5) with H–C(9) (δ 2.24 (br. *t*, $J = 12.5$ Hz, 1 H)), from which we further inferred that H–C(9) was β-oriented. The structure and configuration of **1** was finally confirmed by the single-crystal X-ray-analysis (*Fig. 4*).

An attempt to transform maoecrystal A (**3**) to **1** by acid treatment similar to the reported method [12] was made but did not succeed (see *Exper. Part*): only 15-*O*-deacetyl-maoecrystal A (**4**) was obtained rather than the expected corresponding seco-aldehyde. Compound **1** is an unprecedented example, establishing that a naturally occurring *ent*-abietane diterpenoid can have an oxygenation pattern almost identical to those of *ent*-kaurane diterpenoids. This discovery will be significant and helpful for the deduction of the biotransformation between these two types of diterpenoids. The possibility that this structure is an artifact produced during the extraction and separation procedure can be excluded because the isolation conditions did not involve the use of temperatures above 60° or any acid or alkali.

Compound **2** (*Fig. 1*), colorless crystals from Me_2CO, displayed a molecular-ion peak at *m*/*z* 320, in accordance with a molecular formula $C_{20}H_{32}O_3$, which was verified by analysis of its NMR and DEPT spectra (*Tables 1* and *2*). The IR spectrum of **2**

revealed absorptions for OH groups at 3465 and 3453 cm^{-1} and for a C=C bond at 1640 cm^{-1}. The ^1H,^1H COSY, HMQC, HMBC (*Fig. 2*), and ROESY (*Fig. 5*) experiments, as well as its X-ray crystallographic analysis (*Fig. 6*) allowed us to establish the structure of compound **2** as *ent*-abieta-7,15(17)-diene-3β,16,18-trial, which we name laxiflorin O. By comparison, the structure of **2** was similar to that of eriocaside A, which was the only abietane diterpenoid without aromatic ring C isolated from the *I. eriocalyx* up to now [13]. Except that the C(15)=C(17) bond of **2** was replaced by a diol moiety in eriocaside A, the two compounds have the same skeleton and relative configuration. These similarities prompt us to presume that eriocaside A might also be an *ent*-abietane diterpenoid rather than an abietane diterpenoid, which should be the only situation explicable.

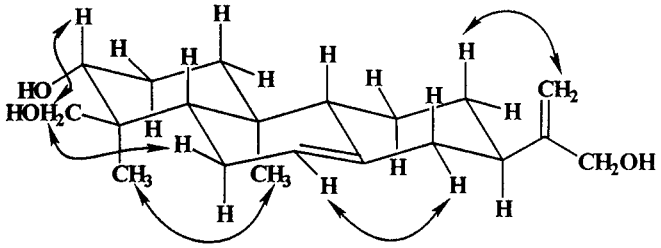


Fig. 5. *Key ROESY correlations of compound* **2**

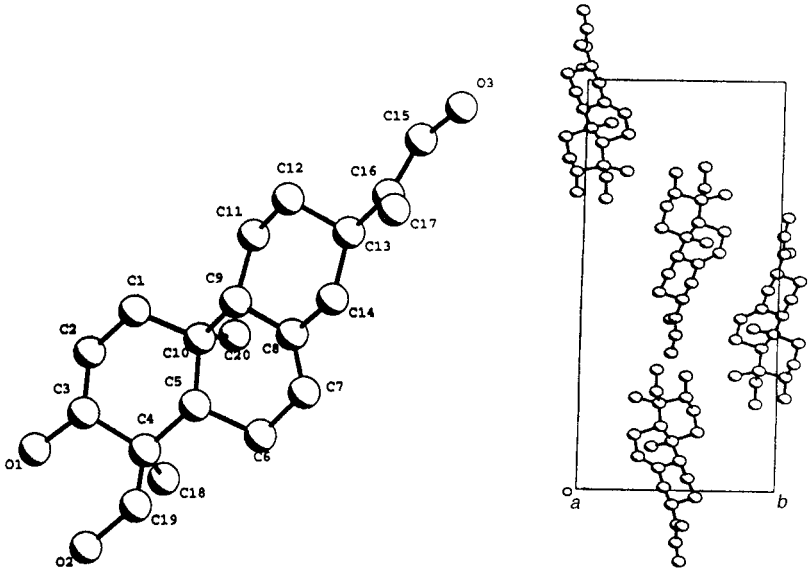


Fig. 6. *X-Ray crystallographic structure of compound* **2**

The ^1H-NMR spectrum of **2** (*Table 1*) showed the presence of two tertiary Me groups (δ 1.14 (*s*, 3 H) and 0.91 (*s*, 3 H)), three olefinic protons (δ 5.45 (*s*, 1 H), 5.04 (*s*, 1 H), and 5.35 (br. *s*, 1 H)), one O–CH_2 *s* at δ 4.43 (*s*, 2 H), one O–CH *t* at δ 4.24 (*t*, J = 8.0 Hz, 1 H), and an *AB* pattern at δ 4.12 (*d*, J = 10.5 Hz, 1 H) and 3.66 (*d*, J = 10.5 Hz, 1 H). The ^{13}C-NMR spectrum (*Table 2*) demonstrated the signals for two Me, six CH_2, two O–CH_2, three CH, one O–CH, two quaternary C-atoms, one olefinic CH_2, one olefinic CH, and two olefinic

quaternary C-atoms. The overall NMR data of **2** was in accordance with the skeleton of an abietane diterpenoid. The signal at δ(H) 4.24 (t, J = 8.0 Hz, 1 H) showed simultaneous long-range couplings with a quaternary C-atom at δ(C) 43.4, a CH at δ(C) 43.1, an O–CH_2 at δ(C) 68.0, and a Me at δ(C) 13.0 in the HMBC spectrum (*Fig. 2*), which suggested that an OH group was located at C(3), and one O–CH_2 was assignable to either C(18) or C(19). The other O–CH_2 was assigned to C(16) according to the HMBC interactions of δ(H) 4.43 (s, 2 H) with the exocyclic methylene C(17) (δ(C) 107.0 (t)). Two olefinic C-atoms at δ(C) 120.7 (d) and 137.4 (s), together with the olefinic proton at δ(H) 5.35 (br. s, 1 H), which was correlated with C(5) at δC(C) 43.1 (d) in the HMBC spectrum, indicated the presence of a C=C bond between C(7) and C(8).

The orientation of H–C(5), H–C(9), and H–C(13) could not be established by the ROESY experiment (*Fig. 5*) since most of the proton signals overlapped. Only the observations of the correlations of H–C(3) (δ 4.24 (t, J = 8.0 Hz, 1 H)) with CH_2(18) (δ 4.12 and 3.66 (d, J = 10.5 Hz, each 1 H)), and of Me(19) (δ 1.14 (s, 3 H)) with Me(20) (δ 0.91 (s, 3 H)) in the ROESY plot indicated that the orientations of H–C(3) and CH_2(18) were opposite to those of Me(19) and Me(20). Considering the biogenesis of compound **1** as *ent*-abietane diterpenoid, probably derived from an *ent*-kaurane diterpenoid, compound **2** should also be an *ent*-abietane diterpenoid, in which H–C(5), H–C(9), H–C(13), and Me(20) have the β,β,α, and α orientation, respectively. On the basis of the above inference, the β-orientation was assigned to H–C(3) and CH_2(18). The structure, relative configuration, and probable absolute configuration of **2** were finally confirmed by X-ray analysis (*Fig. 6*).

Experimental Part

General. Column chromatography (CC): silica gel (200–300 mesh; *Qingdao Marine Chemical Inc.*, China), silica gel *H* (10–40 μ; *Qingdao Marine Chemical Inc.*, China), *Lichroprep RP$_{18}$* gel (40–63 μm; *Merck*, Darmstadt, Germany), *MCI* gel (70–150 μ; *Mitsubishi Chemical Corporation*, Tokyo, Japan); fractions were monitored by TLC, and spots were visualized by heating the silica gel plates sprayed with 10% H_2SO_4 in EtOH. M.p.: *XRC-1* apparatus; uncorrected. Optical rotations: *Horiba SEAP-300* spectropolarimeter. UV Spectra: *Shimadzu 210A* double-beam spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Bio-Rad FTS-135* infrared spectrophotometer; in cm^{-1}. KBr pellets; 1D- and 2D-NMR Spectra: *Bruker AM-400* and *DRX-500* instruments; chemical shifts δ in ppm with reference to the solvent signals, J in Hz. MS: *VG Auto-Spec-3000* spectrometer; m/z (rel. %).

Plant Material. The leaves of *I. eriocalyx* (DUNN) HARA var. *laxiflora* C. Y. WU et H. W. LI were collected in Xishuangbana prefecture, Yunnan Province, People's Republic of China, in November 1999 and identified by Prof. *G. D. Tao*, Xishuangbana Botanic Garden. A voucher specimen has been deposited in the Herbarium of Kunming Institute of Botany, the Chinese Academy of Sciences.

Extraction and Isolation. The dried and powdered leaves (25 kg) were extracted with 70% Me_2CO at r.t. for 3 × 24 h and filtered. The filtrate was concentrated and partitioned with AcOEt. The AcOEt part was evaporated to give 1000 g of a residue, which was subjected to CC (silica gel, 9 × 200 cm, 3000 g); $CHCl_3$, then $CHCl_3$/Me_2CO 9:1, 8:2, and 7:3) and Me_2CO; TLC monitoring): six crude fractions. *Fr. 2* was chromatographed by MPLC (silica gel (800 g), petroleum ether/Me_2CO 4:1, 3:1, 2:1, and 1:1) to give four sub-fractions, the fourth of which was further purified by MPLC (silica gel (100 g), $CHCl_3$/Me_2CO 9:1 and 8:2): **1** (51 mg). *Fr. 3* was further purified by repeated CC (1. silica gel (200 g), petroleum ether/Me_2CO 3:1, 2:1, and 1:1; 2. *MCI-gel CHP-20P* (100 g), H_2O/MeOH 1:1, 4:6, and 0:1; 3. silica gel (100 g), hexane/^{i}PrOH 9:1 and 8:2): **2** (5 mg).

Laxiflorin N (**1**). Colorless crystals (Me_2CO). M.p. 244.0–245.5°. $[\alpha]_D^{15.8} = -68.30$ (c = 0.79, C_5H_5N). UV (H_2O): 204 (4.10). IR (KBr): 3374, 3107, 3005, 2982, 2960, 2934, 2888, 2872, 1742, 1700, 1631, 1478, 1372, 1259, 1219, 1182, 1130, 1090, 1061, 1037, 959, 912, 878, 823, 714, 699, 676, 664. ^{1}H-NMR (C_5D_5N, 500 MHz): *Table 1*. ^{13}C-NMR (C_5D_5N, 125 MHz): *Table 2*. EI-MS (70 eV): 362 (37, M^+), 344 (15), 332 (8), 318 (100), 300 (22), 288 (17), 274 (18), 258 (16), 245 (14), 231 (23), 217 (15), 205 (27), 191 (37), 175 (22), 161 (21), 159 (21), 145 (22), 135 (28), 123 (45), 105 (45), 91 (75), 79 (71), 67 (62). HR-EI-MS: 362.1709 ($C_{20}H_{26}O_6^+$; calc. 362.1729).

X-Ray Crystal-Structure Analysis of **1**[1]). Crystal data: $C_{20}H_{26}O_6$, M 362.42; monoclinic system, space group $P2_1$; a = 7.2600(3), b = 14.2030(5), c = 9.2070(5) Å, β = 108.915 (2)°, V = 898.10(7) Å^3, Z = 2, d = 1.345 g cm^{-3};

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[1]) Crystallographic data (excluding structure factors) for **1** and **2** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition Nos. CCDC-202026 and -202027. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ UK (fax: +44(1223)336033; e-mail: deposit@ccdc.ac.uk).

Mo$K\alpha$ radiation, linear absorption coefficient $\mu = 1.0\ cm^{-1}$. A colorless lumpish crystal of dimensions $0.15 \times 0.15 \times 0.30$ mm was used for X-ray measurements on a *MAC-DIP-2030* diffractometer with a graphite monochromator, the $2\theta_{max}$ value was set at 50.0°. The total number of independent reflections measured was 1607, of which 1604 were considered to be observed ($|F^2 \geq 8\sigma|F|^2$). The structure was solved by the direct method SHELX-86 [14] and expanded with difference *Fourier* techniques, refined by the program and method NOMCSDP [15] and full-matrix least-squares calculations. H-Atoms were fixed at calculated positions. The final indices were $R_f = 0.045$, $R_w = 0.048$ ($w = 1/\sigma M/ZF|^2$), $S = 4.389$, $(\Delta/\sigma)_{max} = 0.153$, $(\Delta\rho)_{min} = -0.200$ e/Å^3, $(\Delta\rho)_{max} = 0.170$ e/Å^3.

Acid Treatment of **1**. Maoecrystal A (**3**; 50 mg) was heated for 10 h in refluxing MeOH (15 ml) containing 2M HCl (15 ml). On cooling, the mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated and then directly subjected to crystallization from Me_2CO to afford 15-*O*-deacetyl-maoecrystal A (**4**). Colorless needles. M.p. 302.5–304.0°. ^{13}C-NMR (C_5D_5N, 125 MHz): *Table 2*. EI-MS (70 eV): 346 (100, M^+), 328 (50), 318 (61), 300 (66), 288 (40), 269 (15), 257 (26), 243 (29), 231 (59), 229 (64), 215 (65), 201 (26), 187 (36), 173 (25), 159 (18), 145 (19), 129 (10), 115 (10), 105 (13), 91 (19), 79 (17), 69 (15), 55 (26).

Laxiflorin O (**2**). Colorless needles (Me_2CO). M.p. 125.0–127.0°. $[\alpha]_D^{15.3} = +23.57$ ($c = 0.35$, MeOH). UV (MeOH): 205.5 (4.13). IR (KBr): 3465, 3453, 2970, 2954, 2887, 1640, 1472, 1453, 1387, 1299, 1252, 1217, 1184, 1138, 1095, 1062, 1022, 1007, 1000, 968, 933, 916, 874, 838. ^{1}H-NMR (C_5D_5N, 500 MHz): *Table 1*. ^{13}C-NMR (C_5D_5N, 125 MHz): *Table 2*. EI-MS (70 eV): 320 (18, M^+), 302 (29), 287 (45), 271 (58), 253 (35), 243 (15), 229 (23), 217 (15), 205 (27), 191 (37), 175 (22), 161 (21), 159 (21), 145 (22), 135 (28), 123 (45), 105 (45), 91 (75), 79 (71), 67 (62), 55 (70). HR-EI-MS: 320.2400 ($C_{20}H_{32}O_3^+$; calc. 320.2351).

X-Ray Crystal-Structure Analysis of **2**[1]). Crystal data: $C_{20}H_{32}O_3$, $M = 320.47$; orthorhombic system, space group $P2_12_12_1$, $a = 6.6150(2)$, $b = 9.9710(5)$, $c = 27.4880(12)$ Å, $V = 1813.06(13)$ Å^3, $Z = 4$, $d = 1.178$ g cm^{-3}; Mo$K\alpha$ radiation, linear absorption coefficient $\mu = 1.0\ cm^{-1}$. A colorless lumpish crystal of dimensions $0.20 \times 0.20 \times 0.40$ mm was used for X-ray measurements on a *MAC-DIP-2030* diffractometer with a graphite monochromator, the $2\theta_{max}$ value was set at 50.0°. The total number of independent reflections measured was 1789, of which 1784 were considered to be observed ($|F|^2 \geq 8\sigma|F|^2$). The structure was solved by the direct method SHELX-86 [14] and expanded with difference *Fourier* techniques, refined by the program and method NOMCSDP [15] and full-matrix least-squares calculations. H-Atoms were fixed at calculated positions. The final indices were $R_f = 0.064$, $R_w = 0.063$ ($w = 1/\sigma|F|^2$), $S = 4.721$, $(\Delta/\sigma)_{max} = 0.108$, $(\Delta\rho)_{min} = -0.270$ e/Å^3, $(\Delta\rho)_{max} = 0.390$ e/Å^3.

REFERENCES

[1] H. D. Sun, Y. L. Xu, B. Jiang, 'Diterpenoids from Isodon Species', Beijing Academic Press, Beijing, 2001.
[2] E. Fujita, M. Node, 'Progress in the Chemistry of Organic Natural Products', 'Diterpenoids of Rabdosia Species', Springer-Verlag, 1984, Vol. *46*, p. 77.
[3] C. Y. Wu, H. W. Li, 'Flora Republicae Popularis Sinicae', Beijing Academic Press, Beijing, 1987, Vol. *66*, p. 494.
[4] Z. Y. Wang, Y. L. Xu, *Acta Botanica Yunnanica* **1982**, 4, 407.
[5] H. D. Sun, Z. W. Lin, F. D. Niu, P. Q. Shen, L. T. Pan, L. Z. Lin, A. C. Geoffrey, *Phytochemistry* **1995**, 38, 1451.
[6] J. Wang, Z. W. Lin, H. D. Sun, *Chin. Chem. Lett.* **1997**, 8, 421.
[7] A. J. Hou, B. Jiang, H. Yang, Q. S. Zhao, Z. W. Lin, H. D. Sun, *Acta Botanic Yunnanica* **2000**, *22*, 337.
[8] C. B. Li, H. D. Sun, J. Zhou, *Acta Chimica Sinica* **1988**, *46*, 657.
[9] J. Wang, Z. W. Lin, Q. S. Zhao, H. D. Sun, *Phytochemistry* **1998**, *47*, 307.
[10] J. Wang, Z. W. Lin, S. Tetsuro, H. D. Sun, *Nat. Prod. Sci.* **1997**, *4*, 143.
[11] X. M. Niu, S. H. Li, Q. S. Zhao, Z. W. Lin, H. D. Sun, Y. Lu, C. Wang, Q. T. Zheng, *Tetrahedron Lett.* **2002**, *43*, 661.
[12] T. Isobe, T. Kamikawa, I. Kubo, T. Kubota, *Bull. Chem. Soc. Jpn.* **1972**, *46*, 583.
[13] X. Y. Shen, A. Isogai, K. Furihata, H. D. Sun, A. Suzuki, *Phytochemistry* **1993**, *34*, 1595.
[14] G. M. Sheldrick, University of Göttingen, Federal Republic of Germany, 1985.
[15] Y. Lu, B. M. Wu, *Chinese Chem. Lett.* **1992**, *3*, 637.

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