Fragrant Volatile Sesquiterpenoids Isolated from the Essential Oil of *Laggera pterodonta* by Using Olfactory-Guided Fractionation

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Chemical composition of the essential oil from *Laggera pterodonta* (Compositae) was inverstigated. GC/MS Analyses led to the identification of 68 components, representing more than 96% of the total oil. By focusing on the woody note fraction of the essential oil, one new bisabolane-type sesquiterpenoid, bisabola-2,7(14),11-trien-10-ol (**1**), together with ten known compounds, bisabolol oxide B (**2**), ylangenol (**3**), copaborneol (**4**), guai-11-en-10-ol (**5**), spathulenol (**6**), aromadendran-10-ol (**7**), caryophyllenol (**8**), 5α,7α-eudesm-11(13)-en-4α-ol (**9**), γ-costic acid (**10**), and eudesma-4(15),11(13)-diene-12,5β-olide (**11**), were isolated by using olfactory-guided fractionation. The structures of the eleven compounds were determined by NMR and MS analyses. All the volatile compounds reported here were isolated for the first time from this plant. On the basis of preliminary odor assessment, the odor of the woody-note fractions of the essential oil was assumed to be due to these isolated sesquiterpenoids.

Introduction. – Essential oils are complex mixtures of volatile compounds isolated from plants by hydrodistillation or steam distillation, and by expression. In addition to the diverse ecological functions of the volatile substances, essential oils and some of their constituents are used not only in pharmaceutical products for their therapeutic activities but also in agriculture, cosmetics and perfumes, and other industrial fields.

During our studies on the chemical compositions (including scent molecules) of aromatic plants from Yunnan, China, the plant *Laggera pterodonta* (DC.) BENTH. from Compositae family was selected for further studies. *L. pterodonta* is widely distributed in southwestern China, especially in Yunnan Province, and it is traditionally employed as ethnomedicine because of its anti-inflammatory and antibacterial activities [1]. Previous work revealed that sesquiterpenes are the major components of the plant, and many new compounds were isolated from it during the last two decades [2][3]. Other types of terpenoids and flavonoids were also isolated from the aerial part of the plant [4]. Meanwhile, *L. pterodonta* was established as an essential-oil bearing plant, and its essential oil relieves cough, reduces sputum, and has antimicrobial activity [1][5]. It was also important with respect to secondary metabolites with bioactivities, which had been rarely studied [5–7], and none of these studies involved the investigation of its fragrant molecules and their possible use in flavor and fragrance industry.

The essential oil of *L. pterodonta* has a fresh herbal, green, laurel-leaf, terpenic, tea-tree, carrot seed odor on smelling strip, while GC-smelling analysis revealed a floral,

marine, woody note in the oil. Linalool was found to be the main compound responsible for the floral odor, while the woody aroma of the oil was attributed to a series of sespuiterpenoid derivatives, of which some could not be identified by GC/MS analysis. Woody notes play a decisive role in modern perfumery, as they form the foundation of several perfumes [8]. In this study, we focused on the constituents responsible for the woody and floral notes of the essential oil, including some minor compounds that exhibited no detectable peaks in GC-mass spectra but may significantly contribute to the whole odor of the oil. Herein, we report the chemical-constituent analysis of the *L. pterodonta* essential oil, as well as isolation and elucidation of the fragrant compounds by olfactory-guided fractionation of the woody note fractions.

Results and Discussion. – *Chemical Composition of the Essential Oil of* L. pterodonta. Qualitative and quantitative analyses of the essential oil by GC/FID and GC/MS led to the identification of 68 components, representing 96.9% of the total oil composition. GC/MS/Olfactory (GC/MS/O) analysis was used to assess and identify woody-note compound peaks, which were mainly distributed in the relatively high-boiling region. In addition, α-terpinene as woody-scent constituent was reported in [9]. The essential-oil composition and the relative amounts of the components are compiled in *Table 1*.

Isolation and Characterization of Main Fragrant Constituents. The essential oil was partitioned into 18 fractions after preliminary separation. *Frs. 14* and *15* were selected for further fractionation on the basis of their obvious woody odor. Direct odor assessment using smelling strips was used to track woody-odor fractions and guided sequential separations. For those fractions isolated from *Frs. 14* and *15* which were regarded as non-woody, comparison of GC analysis of retention times with GC/MS/O data was needed so as to avoid influence of smell-blocking phenomena. Several subfractions with retention indices (*RI*s) from 1700 to 2000 gave rise to peaks, which were too small to be detected.

Olfactory-guided fractionation of the woody-note constituents of the essential oil furnished eleven sesquiterpenoids (*Fig. 1*), including a new bisabolane-type sesquiterpenoid, bisabola-2,7(14),11-trien-10-ol (**1**) with floral and fruity odor, together with ten known compounds. These compounds were isolated from *L. pterodonta* for the first time. By comparing their *RI* values with GC/MS/O data, the previously considered as unknown woody scent peaks in the essential oil were identified as copaborneol (**4**) and guai-11-en-10-ol (**5**).

Structure Elucidation and Olfactory Evaluation of the Isolated Compounds. Compound **1** was obtained as colorless oil. It was assigned the molecular formula $C_{15}H_{24}O$ (four degrees of unsaturation) on the basis of its HR-EI-MS (*m*/*z* 220.1834 (M^+)) and NMR data. The IR spectrum indicated the presence of an OH group (3441 cm^{-1}) and C=C bonds (1637 cm^{-1}). Analysis of the 1D-NMR data revealed the presence of 15 C-atoms, including two Me, seven CH_2 (two sp^2 olefinic; δ(H) 4.90 (*s*) and 4.74 (*s*); δ(C) 107.5 and 110.0), and three CH groups (one O-bearing, δ(H) 4.02 (*dd*), δ(C) 75.3), one olefinic CH group (δ(H) 5.39 (*s*); δ(C) 121.4)), and three olefinic C_q atoms (see *Table 2*). The data indicated that **1** had two terminal C=C bonds and one trisubstituted C=C bond. As these functional groups accounted for three degrees of unsaturation deduced from the molecular formula, **1** had a monocyclic structure. The

Table 1. *Chemical Composition of the Essential Oil from* L. pterodonta

Compounds	*RI*[a])	$RI_{lit.}$[b])	Content [%][c])	Identification[d])
α-Thujene	928	924	0.28	MS, *RI*
α-Pinene	935	932	5.76	MS, *RI*
Camphene	950	946	0.04	MS, *RI*
Thuja-2,4(10)-diene	956	953	0.16	MS, *RI*
Sabinene	975	969	0.61	MS, *RI*
β-Pinene	979	974	0.15	MS, *RI*
Myrcene	991	988	0.16	MS, *RI*
α-Phellandrene	1007	1002	0.07	MS, *RI*
α-Terpinene	1019	1014	0.43	MS, *RI*
p-Cymene	1026	1020	1.27	MS, *RI*
Limonene	1031	1024	0.25	MS, *RI*
1,8-Cineole	1035	1026	15.15	MS, *RI*
(*E*)-Ocimene	1048	1044	0.02	MS, *RI*
γ-Terpinene	1061	1054	1.00	MS, *RI*
(*E*)-Sabinene hydrate	1069	1070[e])	0.09	MS, *RI*
Terpinolene	1091	1086	0.33	MS, *RI*
Linalool	1101	1095	0.54	MS, *RI*
Hotrienol	1105	1104[e])	0.17	MS, *RI*
(*Z*)-*p*-Menth-2-en-1-ol	1124	1118	0.09	MS, *RI*
Campholenic aldehyde	1129	1128[e])	0.06	MS, *RI*
(*E*)-*p*-Menth-2-en-1-ol	1142	1136	0.05	MS, *RI*
(*E*)-Pinocarveol	1143	1135	0.08	MS, *RI*
δ-Terpineol	1170	1162	0.23	MS, *RI*
Terpinen-4-ol	1182	1174	1.68	MS, *RI*
p-Cymene-8-ol	1188	1179	0.07	MS, *RI*
α-Terpineol	1195	1186	2.04	MS, *RI*
Myrtenol	1201	1198	0.10	MS, *RI*
Methyl thymyl ether	1237	1232	0.03	MS, *RI*
Dehydrated geovertol	1292	1289[e])	0.58	MS, *RI*
α-Cubebene	1357	1345	0.41	MS, *RI*
Cyclosativene	1376	1369	0.62	MS, *RI*
Isomer of cyclosativene	1377	–	0.46	MS
α-Copaene	1386	1374	8.40	MS, *RI*
β-Bourbonene	1395	1387	0.24	MS, *RI*
β-Copaene	1398	1430	0.11	MS, *RI*
β-Elemene	1399	1389	0.15	MS, *RI*
7-Episesquithujene	1411	1394	0.33	MS, *RI*
4-Isopropyl-2,5-dimethoxy-1-methylbenzene	1428	1428[e])	7.15	MS, *RI*
(*E*)-Caryophyllene	1431	1417	1.97	MS, *RI*
(*E*)-α-Bergamottene	1443	1432	0.91	MS, *RI*
Geranyl acetone	1456	1453	0.16	MS, *RI*
(*Z*)-Muurola-3,5-diene	1458	1450	0.12	MS, *RI*
Sesquisabinene	1463	1457	0.18	MS, *RI*
α-Humulene	1466	1452	2.05	MS, *RI*
Allo-aromadendrene	1473	1473[e])	0.75	MS, *RI*
α-Acoradiene(tent)	1475	1464	0.11	MS, *RI*
Drim-8(12)-ene	1481	1491	0.16	MS, *RI*
γ-Curcumene	1490	1481	0.59	MS, *RI*
β-Selinene	1500	1489	9.40	MS, *RI*
α-Selinene	1507	1498	0.37	MS, *RI*

Table 1 (cont.)

Compounds	*RI*[a])	$RI_{lit.}$[b])	Content [%][c])	Identification[d])
α-Muurolene	1510	1500	0.31	MS, *RI*
β-Bisabolene	1516	1505	2.97	MS, *RI*
β-curcumene	1519	1514	0.39	MS, *RI*
δ-Cadinene	1534	1522	3.83	MS, *RI*
Caryophyllenol (**8**)	1541	–	t	MS, NMR
α-Calacorene	1555	1544	0.73	MS, *RI*
Z-Sesquisabinene hydrate	1561	1542	0.46	MS, *RI*
(*E*)-Nerolidol	1568	1561	0.12	MS, *RI*
Caryophyllene oxide	1599	1582	3.58	MS, *RI*
Spathulenol (**6**)	1607	1577	t	MS, *RI*, NMR
Caryophyllene oxide	1625	1622[e])	1.18	MS, *RI*
10-epi-γ-Eudesmol	1635	1622	0.47	MS, *RI*
Aromadendran-10-ol (**7**)	1636	–	t	MS, NMR
Copaborneol (**4**)	1640	–	0.63	MS, NMR
α-Cadinol	1658	1652	0.35	MS, *RI*
β-Eudesmol	1665	1662[e])	13.22	MS, *RI*
Ylangenol (**3**)	1670	–	1.21	MS, NMR
β-Bisabolol	1679	1674	0.39	MS, *RI*
Bisabolol oxide B (**2**)	1686	–	t	MS, NMR
Guai-11-en-10-ol (**5**)	1688		t	MS, NMR
Cadalene	1688	1686[e])	0.12	MS, *RI*
5α,7α-Eudesm-11(13)-en-4α-ol (**9**)	1689	–	t	MS, NMR
α-Bisabolol (2,2)	1695	1692[e])	0.69	MS, *RI*
Bisabola-2,7(14),11-trien-10-ol (**1**)	1701	–	t	MS, NMR
γ-Costic acid (**10**)	1881	–	t	MS, NMR
Eudesm-4(15),11(13)-dien-12,5β-olide (**11**)	1939	–	t	MS, NMR
Tricosane	2300	2300	0.05	MS, *RI*
Tetracosane	2400	2400	0.02	MS, *RI*
Pentacosane	2500	2500	0.09	MS, *RI*
Total			96.94	
Monoterpene hydrocarbons			9.26	
Oxygenated monoterpenes			20.28	
Sesquiterpene hydrocarbons			33.85	
Oxygenated sesquiterpenes			22.46	
Phenolic ethers and other types			11.09	

[a]) *RI*, Linear retention indices determined relative to a series of *n*-alkanes (C_8–C_{30}) on the *HP-5* capillary column. [b]) RI_{lit}, *RI* reported by *Adams* [10], determined on an apolar column, except those marked with [e]), which are included in the *Givaudan* database. [c]) Relative content determined by FID peak-areas; t, traces (≤ 0.01). [d]) Identification of the compounds: MS, comparison of mass spectra with those listed in NIST08 mass-spectral libraries; *RI*, comparison of *RI* with those of authentic samples or from the literature; NMR, compound was isolated and characterization by NMR spectroscopy. [e]) *RI* from the *Givaudan* database.

^{1}H- and ^{13}C-NMR spectra of **1** were very similar to those of helianthol A [11], with the significant difference being observed for C(10)–C(12). A terminal C(11)=C(12) bond was confirmed by HMBCs of the singal at δ(H) 4.74 (*s*, 1 H) with those at δ(C) 149.3 (*s*), 17.8 (*q*, C(15)), and of the singal at δ(H) 1.66 (*s*, Me(15)) with that δ(C) 110.0 (*t*).

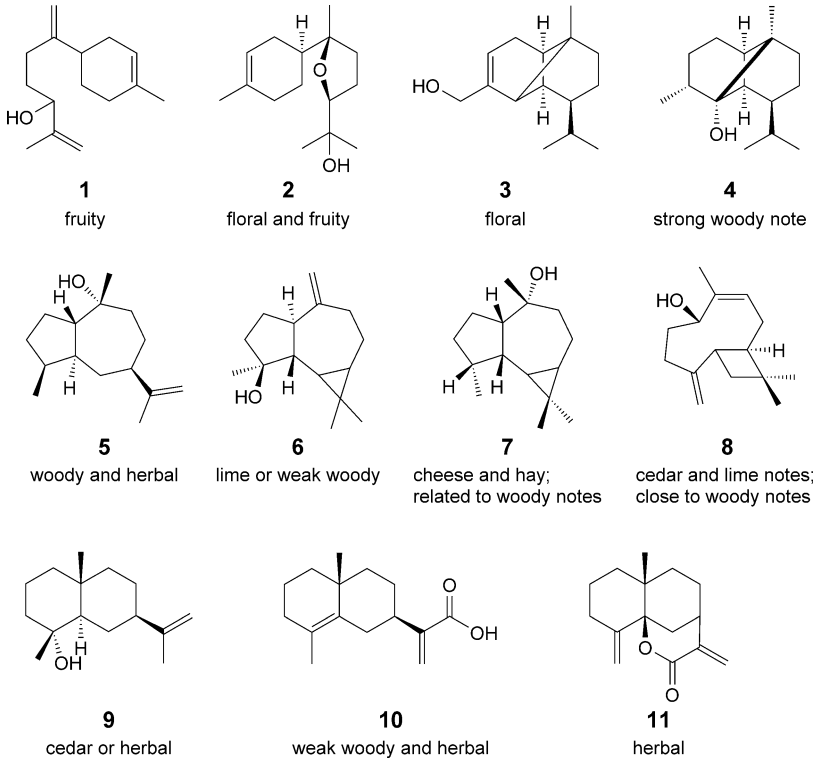

Fig. 1. *Compounds isolated from the essential oil of* L. pterodonta

The presence of the OH group at C(10) was corroborated by means of COSY correlations between the signals at δ(H) 2.00–2.02 (*m*, CH_2(8)) and 1.61–1.65 (*m*, CH_2(9)); those at δ(H) 1.61–1.65 and 4.02 (*dd*, 1 H), and HMBCs of the signal at δ(H) 1.66 (*s*, Me(15)) with that at δ(C) 75.3 (*d*); of the signal at δ(H) 4.02 (*dd*, 1 H) with those at δ(C) 110.0 (*t*, C(12)), 17.8 (*q*, C(15)), 149.3 (*s*, C(11)) (*Fig. 2*). The absolute configuration of **1** remained unassigned. Due to the large interatomic distances between the stereogenic center C(6) of the cyclohexene ring and the stereogenic C-atom C(10), it was impossible to determine the relative configuration by using NOESY data. Hence, the structure of **1** was elucidated as bisabola-2,7(14),11-trien-10-ol (**1**).

The known sesquiterpenoids isolated from the woody-note fraction of the essential oil of *L. pterodonta* were identified as bisabolol oxide B (**2**) [12], ylangenol (**3**) [13],

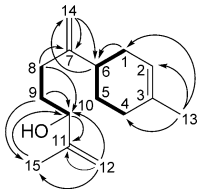

Fig. 2. *^{1}H,^{1}H-COSY* (—) *and HMB* (H→C) *correlations of* **1**

Table 2. *^{1}H- and ^{13}C-NMR Data of* **1** *Isolated from the Essential Oil of* L. pterodonta (recorded in (D_6)acetone; δ in ppm, J in Hz)

Position	δ(H)[a])	δ(C)[b])
1	1.41–1.46 (*m*, H_a), 1.76–1.80 (*m*, H_b)	29.5
2	5.39 (*s*)	121.4
3	–	134.0
4	1.83–1.86 (*m*)	32.0
5	2.03–2.07 (*m*)	31.2
6	2.08–2.10 (*m*)	40.6
7	–	155.2
8	2.00–2.02 (*m*)	31.7
9	1.61–1.65 (*m*)	34.8
10	4.02 (*dd*, J=5.2, 11.2)	75.3
11	–	149.3
12	4.90 (*s*, H_a), 4.74 (*s*, H_b)	110.0
13	1.61 (*s*)	23.5
14	4.74 (*s*)	107.5
15	1.66 (*s*)	17.8

[a]) Recorded at 400 MHz. [b]) Recorded at 100 MHz.

copaborneol (**4**) [14], guai-11-en-10-ol (**5**) [15], spathulenol (**6**) [16], aromadendran-10-ol (**7**) [17], caryophyllenol (**8**) [18], 5α,7α-eudesm-11(13)-en-4α-ol (**9**) [19], γ-costic acid (**10**) [20], and eudesma-4(15),11(13)-dien-12,5β-olide (**11**) [21] by comparision of their NMR and MS data with those reported in literature.

The scents of these compounds were evaluated individually. The odor of **4** and **5** was assessed as woody. Compound **4** showed a woody intensity stronger than the rest of the compounds, indicating that it is the main contributor to woody scent fractions. Compound **5** was reported for the first time to emit woody scent. Although other compounds did not display obvious woody scents, they were indispensable for the unique woody scent of *L. pterodonta* oil. Since the odors of **7**–**10**, were similar to woody notes (cheese or hay of **7** [22], cedar of **8**, lime of **9**, and herbal of **10**), these compounds can be regarded as woody-scent-related components. Compounds **1**–**3** emit pleasant fruity or floral odors, which make the woody note more enjoyable. These types of note can be recognized as having odor-enriching function. The odorous characters of these compounds are included in *Fig. 1*.

Conclusions. – In the present study, a series of fragrant compounds was found in *L. pterodonta* essential oil, especially some minor constituents playing significant roles in floral-woody note characteristics. Guaiane-type sesquiterpenoids might be a new type of woody-note compounds. Structural modification studies of this type of compounds may be envisaged to find more active woody-note compounds. Essential oils which do not possess good odor or are only used as medicine, may contain novel fragrant compounds as well. Studies on pharmaceutically used essential oils might lead to the discovery of new scent molecules. If a good method to remove unpleasant-smell components can be developed, *L. pterodonta* essential oil might be a potential natural

source of woody notes, introducing this important traditional Chinese medicinal plant into flavor and fragrance industry.

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Experimental Part

General. TLC: SiO_2 *GF254* (*Qingdao Marine Chemical Co., Ltd.*, P. R. China); visualization by heating SiO_2 plates and sprayed with 10% H_2SO_4. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh, *Qingdao Marine Chemical Co., Ltd.*, P. R. China). Optical rotations: *Horiba Sepa-300* polarimeter. UV Spectra: *Shimadzu UV-2401A* spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Brucker Tenor-27* spectrophotometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker AM-400*, *Bruker DRX-500*, and *Avance III 600*, with Me_4Si as internal standard; δ in ppm rel. to the solvent signals, *J* in Hz. EI- and HR-EI-MS: *Waters AutoSpec Premier P776* spectrometer; in *m*/*z* (rel. %).

Plant Material. The essential oil was extracted by steam distillation from the aerial part of *L. pterodonta* and provided by *Yunnan PanLongYunhai Pharmaceutical Company, Ltd*.

GC/FID and GC/MS/O Analyses. To target woody note peaks, the GC/FID and GC/MS/O analyses of the essential oil were carried out with an *Agilent 7890A* gas chromatograph equipped with an *HP-5* (5% diphenyl polysiloxane) cap. column (50 × 0.32 mm i.d.; film thickness, 0.52 μm). The column effluent was split equally among an *Agilent 5975C* inert mass-selective detector (MSD; ionization potential, 70 eV), an FID detector, and a specially modified *Gerstel* odor-detection port (ODP2) *via* a cap. flow technology splitter plate. The oven temp. was programmed from 60 to 280° at a constant 5°/min and then held isothermal at 280° for 16 min; injector temp., 250°; FID temp., 300°; MSD transfer-line temp., 280°; carrier gas, He (3.26 ml min^{-1}); initial head pressure, 146 kPa. All injections were performed in splitless mode. Data were acquired and processed using MSD ChemStation software.

Olfactory-Guided Fractionation. Olfactory-guided fractionation was performed before each isolation experiment and consisted of two parts: *i*) fractions were dissolved in hexane at a concentration of 2% (*v*/*v*), and then a smelling strip was used for direct assessments. Woody-scent fractions were selected by human olfactory organoleptic results; *ii*) in the case of other blocking smells, non-woody-scent portions were analyzed by GC/FID by means of essential oil spectrum retention time comparison. Either only woody-scent or targeted peaks (with fractions) were isolated.

Extraction and Isolation. The initial essential oil (98.5 g) of *L. pterodonta* was subjected to CC (SiO_2 (70 cm × 8 cm); petroleum ether (PE)/AcOEt 100 : 0, 97 : 3, 95 : 5, 90 : 10, 80 : 20) to yield 18 fractions, *Frs. 1–18*. *Frs. 14* (4.0 g), *15* (5.2 g), and *17* (4.5 g) were identified as woody-odorous fractions. *Fr. 14* was separated into six subfractions, *Frs. 14.1–14.6*, by CC (SiO_2; PE/Et_2O 9 : 1). *Fr. 14.4* (900 mg) was subjected to CC (SiO_2; $CHCl_3$/Et_2O 40 : 1); and *Sephadex LH-20*; acetone) to give **4** (10 mg), **1** (7 mg), and **11** (15 mg). Compounds **2** (20 mg) and **7** (9 mg) were obtained after CC (SiO_2; PE/$CHCl_3$ 4 : 1) and CC on *LH-20* (acetone) followed by CC (SiO_2; PE/Et_2O 9 : 1) from *Fr. 14.5*. *Fr. 15* was divided into five subfractions, *Frs. 15.1–15.5*, by CC (SiO_2; PE/acetone 40 : 1). From *Fr. 15.1*, **5** (20 mg), **6** (12 mg), and **10** (8 mg) were isolated after CC (*Sephadex LH-20*; acetone; and SiO_2; $CHCl_3$/acetone 40 : 1). In the same way, **8** (15 mg), **3** (7 mg), and **9** (7 mg) were obtained from *Frs. 15.2* and *15.3*, resp.

Bisabola-2,7(14),11-trien-10-ol (=*2-Methyl-6-(4-methylcyclohex-3-en-1-yl)hepta-1,6-dien-3-ol*; **1**). Colorless oil. $[\alpha]_D^{14} = -57.03$ ($c = 0.54$ mg/ml, MeOH). UV (MeOH): 202 (0.73). IR: 3441 (OH), 1637 (C=C). ^1H- and ^{13}C-NMR: see *Table 2*. EI-MS: 220 (3.0, M^+), 202 (26.4), 159 (38.3), 134 (100), 119 (98.6), 91 (91.0), 79 (87.4), 41 (57.3). HR-EI-MS: 220.1834 (M^+, $C_{15}H_{24}O^+$; calc. 220.1827).

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