A Novel Meroterpene from *Eurycorymbus cavaleriei*

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A novel symmetric dimeric compound, cavalerol (**1**), was isolated from the 95% EtOH extract of the twigs of *Eurycorymbus cavaleriei*. Compound **1** contains an unprecedented dimeric skeleton with two identical chiral meroterpene moieties.

Introduction. – *Eurycorymbus cavaleriei* (LÉVL.) REHD. et HAND.-MAZZ. is a dioecious, rare, and endemic tree species in P. R. China, and there is only one species in this genus [1]. The tissue culture, genetic diversity, and properties of *Eurycorymbus cavaleriei* have been previously studied [2–7], but few investigations on its chemistry have been reported up to now. A novel meroterpene **1**, which showed medium activity, was obtained from the 95% EtOH extract of the twigs of *Eurycorymbus cavaleriei*.

Results and Discussion. – Compound **1** showed a quasimolecular-ion peak at *m/z* 681 ($[M-H]^-$) in the ESI-MS. The IR absorption at 3397, 1658, and 1453 cm^{-1} suggested the presence of an OH group, a CHO group, and an aromatic chromophore in its structure. The presence of only 22 C-atom signals in the ^{13}C-NMR spectrum, combined with ESI-MS data, indicated that **1** was a dimeric and C_2-symmetric structure with the molecular formula $C_{44}H_{58}O_6$, implying 16 degrees of unsaturation. The ^{1}H- and ^{13}C-NMR (*Table*), HMBC (*Table*), ^{1}H,^{1}H-COSY, and NOESY data (*Fig.*) of **1** and comparison of its optical rotation with that of a known compound [8] established the structure of **1** as 5,5′-dihydroxy-4,4′-bis[(2*S*,4*Z*)-6-hydroxy-5-methyl-2-(1-methylethenyl)hex-4-en-1-yl]-6,6′-bis(3-methylbut-2-en-1-yl)[1,1′-biphenyl]-2,2′-dicarboxaldehyde, which was named cavalerol.

In the downfield region of the ^{1}H-NMR spectrum of **1**, the signals of a CHO group at δ 9.81 (*s*), a terminal $CH_2{=}C$ group at δ 4.75 and 4.66 (2 br. *s*), an olefinic H-atom at δ 5.30 (*t*, $J = 7.2$ Hz), and an aromatic H-atom at δ 7.51 (*s*) were observed. In the upfield region, four Me-group *s* were discernible at δ 1.82 (6 H), 1.64 (3 H), and 1.70 (3 H). The presence of a γ,γ-dimethylallyl group in **1** was inferred from the broad *s* at δ 1.82 (6 H), the two broad *s* at δ 3.41 (1 H) and 3.42 (1 H), and the *t* at δ 5.30 ($J = 7.2$ Hz, 1 H) in the ^{1}H-NMR spectrum, as well as from the signals at δ 131.3 (C(3a)), 120.7 (C(2a)), 29.6 (C(1a)), 25.8 (C(4a)), and 18.0 (C(5a)) in the ^{13}C-NMR spectrum [9]. The ^{1}H-NMR spectrum of **1** also showed the presence of a 6-hydroxylavandulyl group with signals at δ 1.64 (*s*, Me), 1.70 (*s*, Me), 2.16–2.19 (*m*, CH_2), 2.49–2.52 (*m*, CH), 2.73–2.75 (*m*, 2 H), 4.66 and 4.75 (2 br. *s*, $CH_2{=}C$), and 5.37 (*t*, $J = 7.2$ Hz, CH) [8]. The signals at δ(H) 3.99 (*s*, CH_2) and δ(C) 68.9, and the long-range correlation between H–C(4b) and C(6b) in the HMBC experiment indicated that there was an OH group at C(6b). The absolute configuration of C(2b) and C(2b) of **1** was determined as (*S*) by measuring the optical rotation

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of $[\alpha]_D = +20.5$ ($c = 0.060$, MeOH) and comparing it with that of a similar compound [8]. Thus, compound **1** is not a *meso* form, but possesses C_2 symmetry. In the HMBC plot, the δ(H) of the CH_2 group of the γ,γ-dimethylallyl group at 3.42 was correlated with the three aromatic C-atoms at δ(C) 136.6 (C(2)), 130.1 (C(3)), and 158.5 (C(4)) (*Table*). Consequently, C(3) was substituted by the γ,γ-dimethylallyl group. The δ(H) of the CH_2 group of the 6-hydroxylavandulyl group at 2.73 – 2.75 correlated with the three aromatic C-atoms at δ(C) 158.5 (C(4)), 128.1 (C(5)), and 129.3 (C(6)), which suggested that the 6-hydroxylavandulyl group was attached to C(5). The δ(H) of H–C(1c) at 9.81 displayed correlations with the two C-atom signals at δ(C) 136.6 (C(2)) and 129.3 (C(6)), leading to the conclusion that the CHO group is positioned at C(1). Combined ^{13}C-NMR and HR-ESI-MS evidence allowed to place the phenolic OH group at C(4) (158.4). The structure of compound **1** was further supported by ^{1}H,^{1}H-COSY and NOESY data (*Fig.*).

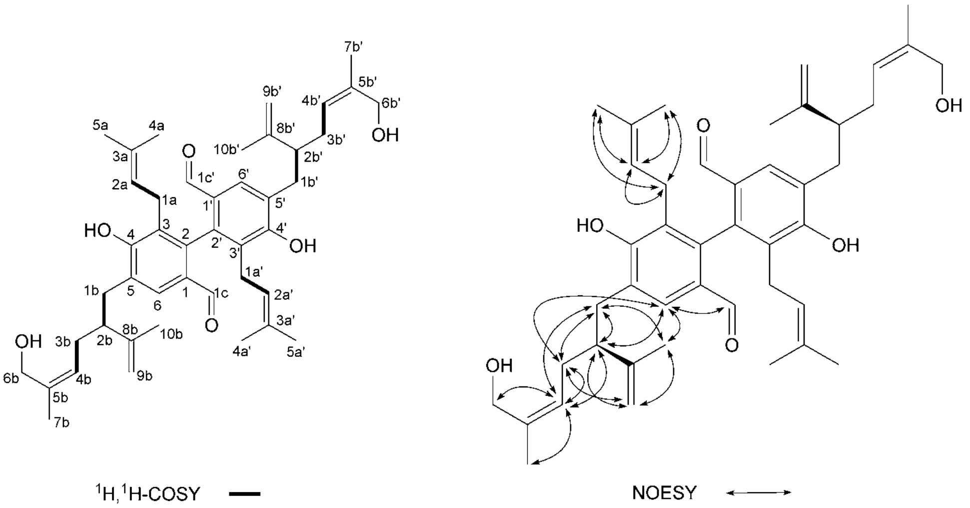

Figure. *^{1}H,^{1}H-COSY and NOESY Correlations of compound* **1**. Arbitrary atom numbering.

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Experimental Part

General. Prep. HPLC: *Agilent-1100* system; photodiode array detector; *Zorbax-C$_{18}$* column (*ODS*, 250 × 21.2 mm, 7 μm). Optical rotations: *Jasco P-1010* polarimeter. UV Spectrum: *Jasco V-550*; λ_{max} in nm. IR Spectrum: *Jasco FTIR-4100*; in cm^{-1}. 1D- and 2D-NMR (HSQC, HMBC, COSY, NOESY) Spectra: *Bruker 600* NMR spectrometer; δ in ppm, J in Hz. EI-MS: *Jeol JMS-SX-102A* mass spectrometer; in *m/z*. ESI-MS: *LCQ-DECA-Thermo-Finnigan* system equipped with a hot ESI source (HESI, electrospray voltage 3.0 kV, sheath gas N_2, vaporizer temp. 50°, capillary temp. 250°, collision gas Ar, collision pressure 1.5 mTorr); in *m/z*.

Plant Material. The twigs of *Eurycorymbus cavaleriei* (LEVL.) REHD. et HAND.-MAZZ. were collected in Yuanlin, Hunan Province, P. R. China, in September 2007. The plant material was identified by the authors. A voucher specimen (No. EC070901) was deposited with the College of Pharmaceutical Sciences, Zhejiang University, P. R. China.

Extraction and Isolation. The air-dried pieces of the twigs (15.0 kg) were extracted with 95% EtOH (3 × 45 l). The crude extract was suspended in distilled H_2O, and the suspension was extracted successively with petroleum ether (3 × 1 l), CH_2Cl_2 (4 × 1 l), AcOEt (4 × 1 l), and BuOH (3 × 1 l). The petroleum ether fraction (30 g) was subjected to column chromatography (silica gel, petroleum ether/

Table. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$; 600 and 150 Hz, resp.) *of Compound* **1**. Arbitrary atom numbering (see *Fig.*).

	δ(H)	δ(C)	HMBC (H → C)
C(1)	–	129.6	–
C(2)	–	136.6	–
C(3)	–	130.1	–
C(4)	–	158.5	–
C(5)	–	128.1	–
H–C(6)	7.51 (*s*)	129.3	C(2), C(4), C(1b), C(1c)
CH_2(1a)	3.41 (*d*, *J* = 7.2)	29.6	C(2), C(3), C(4), C(2a), C(3a)
H–C(2a)	5.30 (*t*, *J* = 7.2)	120.7	C(1a), C(4a), C(5a)
C(3a)	–	131.3	–
Me(4a)	1.82 (*s*)	25.8	C(5a)
Me(5a)	1.82 (*s*)	18.0	C(4a)
CH_2(1b)	2.73–2.75 (*m*)	34.2	C(4), C(5), C(6), C(2b), C(3b), C(8b)
H–C(2b)	2.49–2.52 (*m*)	46.9	C(5), C(1b), C(3b), C(4b), C(8b), C(9b), C(10b)
CH_2(3b)	2.16–2.19 (*m*)	31.1	C(2b), C(4b), C(8b)
H–C(4b)	5.37 (*t*, *J* = 7.2)	124.3	C(6b), C(7b)
C(5b)	–	135.8	–
CH_2(6b)	3.99 (*s*)	68.9	C(4b), C(5b), C(7b)
Me(7b)	1.64 (*s*)	13.9	C(4b), C(5b), C(6b)
C(8b)	–	147.3	–
CH_2(9b)	4.75, 4.66 (2 br. *s*)	111.9	C(2b), C(8b), C(10b)
Me(10b)	1.70 (*s*)	19.6	C(2b), C(8b), C(9b)
H–C(1c)	9.81 (*s*)	191.4	C(2), C(6)

AcOEt 100 : 30 (*v*/*v*)) to afford a complex mixture, which was purified by gel chromatography and then subjected to reversed-phase HPLC ($MeCN/H_2O$ 65 : 35): *5,5′-dihydroxy-4,4′-bis[(2*S*,4*Z*)-6-hydroxy-5-methyl-2-(1-methylethenyl)hex-4-en-1-yl]-6,6′-bis(3-methylbut-2-en-1-yl)-1,1′-biphenyl-2,2′-dicarboxaldehyde (= cavalerol*; **1**; 10 mg, t_R 17.9 min). Yellow oil. $[\alpha]_D = +20.5$ ($c = 0.060$, MeOH). UV (MeOH): 194, 230, 290. IR (KBr): 3397, 2946, 2833, 2218, 2043, 1658, 1453, 1114, 1026, 655. ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS: 681 ($[M-H]^-$). HR-EI-MS: 681.4127 (M^-, $C_{44}H_{57}O_6^-$; calc. 681.4155).

REFERENCES

[1] L. K. Fu, J. M. Jin, in 'China Plant Red Data Book – Rare and Endangered Plants 1', New York Science Press, Beijing, 1992, p. 558.

[2] M. Liao, Z. R. Zhu, X. L. Wei, T. X. Jin, *Seed* **2005**, *24*, 9.

[3] J. Chen, Y. Wang, M. Kang, J. Zhou, H. Huang, *Mol. Ecol. Notes* **2006**, *6*, 160.

[4] L. M. Zhao, X. T. Liang, L. N. Li, *J. Chin. Pharm. Sci.* **1997**, *6*, 111.

[5] J. Wang, Q. G. Ye, M. Kang, H. W. Huang, *Conserv. Genet.* **2008**, *9*, 559.

[6] C. L. Chen, *J. Fujian Forest. Sci. Technol.* **2002**, *29*, 50.

[7] Q. Q. Zhang, W. S. Wu, J. Q. Liu, *J. Fujian Norm. Univ.* (*Nat. Sci.*) **1995**, *11*, 79.

[8] T. H. Kang, S. J. Jeong, W. G. Ko, N. Y. Kim, B. H. Lee, I. Masanori, M. Tomofumi, H. Ryuichi, Y. C. Kim, *J. Nat. Prod.* **2000**, *63*, 680.

[9] S. S. Kang, J. S. Kim, K. H. Son, H. W. Chang, H. P. Kim, *Fitoterapia* **2000**, *71*, 511.

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