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Vielopsides A-E, five new guaiane-type sesquiterpenoid dimers from *Xylopia vielana*

Yang-Guo Xie[a], Guo-jing Wu[a], Tao-fang Cheng[a], Sheng-lan Zhu[a], Shi-kai Yan[a], Hui-zi Jin[a,*], Wei-dong Zhang[a,b,*]

[a] Shanghai Key Laboratory of Antimicrobias, New Drug Discovery, School of Pharmacy, Shanghai Jiao Tong University, Shanghai 200240, PR China
[b] School of Pharmacy, Second Military Medical University, Shanghai 200433, PR China

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ABSTRACT

Five new guaiane-type sesquiterpenoid dimers vielopsides A-E, connecting patterns through two direct C—C bonds (C-2 to C-2′, C-4 to C-1′), were isolated from the roots of Xylopia vielana. Their absolute configurations were established by NOE analysis, the Cu Kα X-ray crystallographic and circular dichroism (CD) experiment. Among them, compound **5** showed moderate activity IC_{50} values of 33.8 μM on NO production in RAW 264.7 macrophages.

1. Introduction

The first phytochemical investigation of the genus *Xylopia* was traced back to 1982 [1]. Several diterpene adducts were isolated from *X. emarginata* and *X. amazonica* [2]. In a continuous research of the genus *Xylopia*, diverse bioactive components, such as alkaloids [3, 4], flavonoids [5], diterpenes [6], and sesquiterpene dimmers [7–9] were obtained. The leaves and roots of the plant have been used as a folk medicine for the treatment of antispasmodic disease, rheumatism, pain and malaria [10]. These results spurred us to further investigate the bioactive compounds from the genus *Xylopia*. Thus, we selected the roots of *X. vielana*, leading to the isolation of five new guaiane-type sesquiterpenoid dimers vielopsides A-E (Fig. 1). Herein, we reported its structural elucidation using 1D and 2D-NMR, X-ray analysis and CD experiments.

2. Results and discussion

Compound **1** was obtained as colorless needle crystals. It was assigned to have the molecular formula $C_{30}H_{36}O_6$ in accordance with HR-ESI: *m/z* 515.2418 $[M + Na]^+$ (calcd for $C_{30}H_{36}O_6Na^+$, 515.2404) analysis, indicating 13 degrees of unsaturation. The ^{13}C NMR and DEPT spectrum showed 30 carbon signals, including eight methyls, three methylenes, four methines and 15 quarternary carbons (Table 1). The ^1H NMR spectrum of **1** also gave corresponding proton signals: six methyls (singlets), two methyls (doublets), three methylenes (multiplets), one olefinic (singlets) and four methane (multiplets). In combination with 2D-NMR suggested **1** displayed the presence of two asymmetry guaiane units (a and b). In HMBC spectrum, the cross-peaks from H-2 to C-1/C-4 and from H_3–15 to C-3/C-4/C-5 (Fig. 2) in unit **1**a indicated that **1** possessed a five-membered ring (I). The presence of the seven-membered ring (II), connected with the five-membered (I) via a C-1/C-5 double bond, which was demonstrated by the HMBC cross-peaks from H-6 to C-1/C-7/C-8/, from H-10 to C-1/C-8/C-9, from H_2-9 to C-1/C-8/C-10 and H_3-14 to C-1/C-9/C-10 (Fig. 2). Furthermore, the HMBC correlations from H-6 to C-7/C-8/C-11/, from H_3-12 to C-11/C-7 and H_3-13 to C-11/C-7 indicated an another five-membered ring (III) was fused with the seven-membered ring (II) through a C-7/C-8 single bond (Fig. 2). The presence of a double oxygen bridge in the five-membered ring (III) was on the basis of the chemical shift of C-8 (δ_C 102.8) and C-11 (δ_C 85.7). So based on the above analysis, the unit **1**a was assigned as a guaiane-type sesquiterpenoid.

Similarly, unit **1**b was also assigned as a guaiane-type sesquiterpenoid. The key HMBC correlations from H_3–15 to C-1′, and H-2 to C-2′ as well as the ^1H-^1H-COSY correlations (Fig. 2) from H-2/H-2′ indicated that units a and unit b should be linked via two direct C—C bonds (C-2 to C-2′, C-4 to C-1′) (Fig. 2). Accordingly, the planar structure of **1** was confirmed as shown in Fig. 2. The relative configuration was deduced by the NOESY experiments. The key NOE correlations of H-2′/H_3-14′, H-2/H_3-14, H-2′/H-2 implied same side similarity and were arbitrarily assigned as *α*-oriented, while the correlations of H-10′/H_3–15′ placed them on the opposite side. (Fig. 3). It was difficult to determine the

* Corresponding authors at: Shanghai Key Laboratory of Antimicrobias, New Drug Discovery, School of Pharmacy, Shanghai Jiao Tong University, Shanghai 200240, PR China.
E-mail addresses: kimhz@sjtu.edu.cn (H.-z. Jin), wdzhangy@hotmail.com (W.-d. Zhang).

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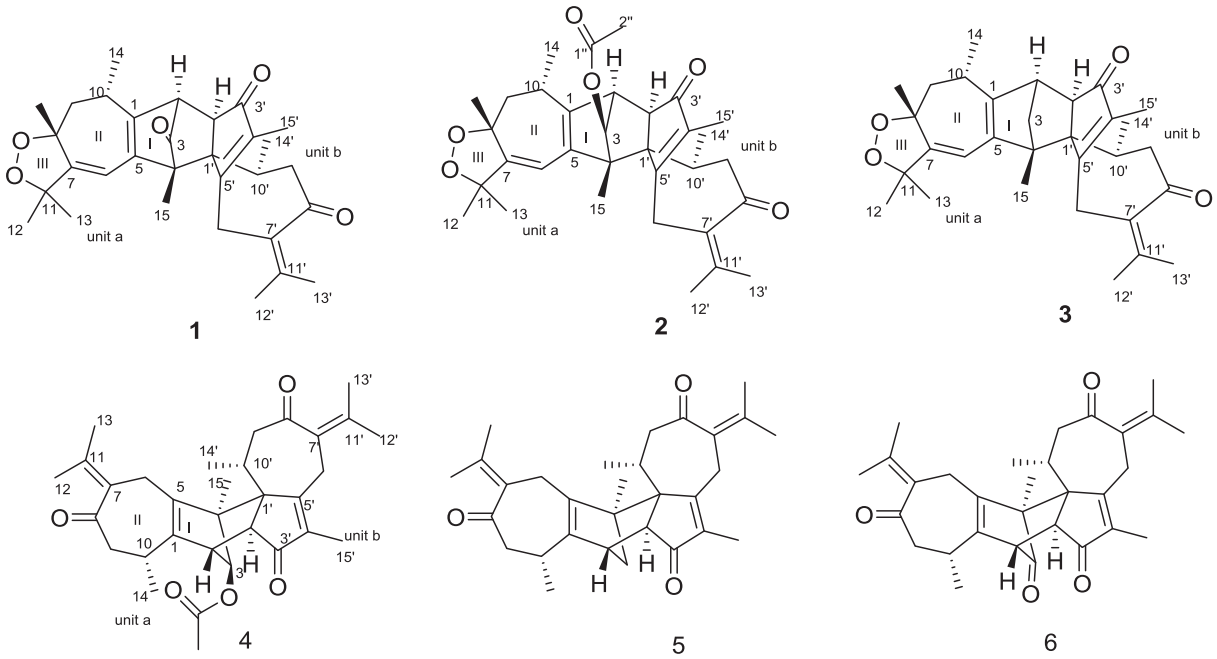

Fig. 1. Chemical structures of compounds **1–6.**

Table 1
^{1}H and ^{13}C NMR spectroscopic data of **1–5**.

No	**1**[a]		**2**[b]		**3**[c]		**4**[d]		**5**[d]	
	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	143.2 s		144.3 s		148.6 s		141.4 s		144.9 s	
2	46.3 d	2.79 d (5.1)	48.3 d	3.18 dd (5.0, 1.9)	46.5 d	3.16 m	47.9 d	2.94 m	45.8 d	2.90 m
3	201.4 s		89.5 d	4.49 d (2.0)	55.1 t	1.98 m 1.50 m	90.1 d	4.53 d (2.0)	56.2 t	1.95 dd (8.5, 1.6) 1.48 dd (8.5, 1.8)
4	57.9 s		56.8 s		56.6 s		58.7 s		58.3 s	
5	132.2 s		132.7 s		134.9 s		137.4 s		139.6 s	
6	109.1 d	5.46 s	111.2 d	5.62 s	110.5 d	5.70 s	25.8 t	3.25 d (16.6) 3.87 d (16.6)	25.4 t	3.18 d (17.0) 2.70 d (17.0)
7	158.5 s		155.6 s		154.8 s		134.4 s		134.5 s	
8	102.8 s		105.2 s		103.1 s		203.6 s		204.1 s	
9	38.2 t	1.93 m 1.63 t (13.3)	33.7 t	2.11 m 1.55 m	37.6 t	1.85 m 1.51 m	47.6 t	2.51 m	47.8 t	2.46 m
10	31.8 d	2.54 m	30.5 d	2.10 m	30.8 d	2.27 m	32.9 d	2.94 m	32.5 d	2.24 m
11	85.7 s		85.3 s		84.5 s		141.0 s		140.4 s	
12	27.3 q	1.37 s	27.5 q	1.39 s	26.9 q	1.35 s	22.9 q	2.01 s	22.5 q	1.97 s
13	23.9 q	1.41 s	24.1 q	1.46 s	23.3 q	1.48 s	22.5 q	1.85 s	22.1 q	1.84 s
14	17.7 q	1.15 d (7.1)	18.6 q	1.14 d (6.9)	18.2 q	1.16 d (7.2)	19.3 q	1.01 d (7.0)	19.4 q	1.00 d (6.9)
15	9.2 q	1.52 s	13.7 q	1.63 s	15.1 q	1.61 s	14.5 q	1.59 s	16.1 q	1.52 s
1′	58.3 s		62.1 s		62.2 s		62.3 s		62.4 s	
2′	52.3 d	3.45 d (5.0)	56.2 d	3.13 m	55.9 d	3.08 m	55.7 d	3.11 m	54.7 d	2.78 m
3′	206.6 s		209.1 s		209.3 s		207.6 s		208.1 s	
4′	144.8 s		141.9 s		140.4 s		141.9 s		140.2 s	
5′	171.6 s		173.2 s		175.2 s		171.8 s		173.4 s	
6′	28.6 t	3.26 d (15.9) 3.05 d (15.9)	30.9 t	3.49 d (14.4) 3.05 d (14.4)	29.5 t	3.45 d (14.8) 3.13 d (14.8)	30.6 t	3.57 d (14.0) 3.02 d (14.0)	29.6 t	3.32 d (14.6) 3.05 d (14.6)
7′	132.2 s		128.5 s		130.9 s		128.9 s		131.3 s	
8′	206.5 s		204.1 s		205.1 s		201.7 s		204.0 s	
9′	49.3 t	2.27 dd (18.6, 2.7) 2.04 dd (18.6, 12.4)	47.9 t	3.41 dd (12.1, 2.7) 2.28 dd (12.1, 6.4)	49.3 t	2.89 m 2.14 dd (15.4, 9.5)	48.3 t	3.36 m 2.33 m	50.1 t	2.62 dd (16.5, 2.3) 2.20 m
10′	29.6 d	2.74 m	33.1 d	2.96 m	32.3 d	2.70 m	32.8 d	2.20 m	31.6 d	2.68 m
11′	138.9 s		146.0 s		141.7 s		145.9 s		140.2 s	
12′	21.6 q	1.77 s	22.9 q	2.06 s	21.4 q	1.89 s	23.6 q	2.12 s	22.8 q	1.85 s
13′	20.3 q	1.81 s	22.6 q	1.93 s	21.0 q	1.91 s	23.4 q	1.97 s	22.7 q	1.90 s
14′	16.4 q	0.90 d (6.8)	16.4 q	0.85 d (7.0)	17.5 q	1.01 d (6.9)	17.2 q	0.89 d (7.0)	19.4 q	1.06 d (6.9)
15′	7.4 q	1.48 s	6.9 q	1.47 s	6.7 q	1.37 s	7.7 q	1.51 s	7.5 q	1.46 s
1″			170.2 s				170.1 s			
2″			20.4 q	2.10 s			21.2 q	2.08 s		

δ in ppm; J in Hz within parentheses; Measured at 125 MHz for ^{13}C NMR and 500 MHz for ^{1}H NMR in [a]Chloroform-*d*: MeOH 1:2; [b]Chloroform-*d*: MeOH 1:3; [c]CD_3OD; [d]Chloroform-*d*.