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Terpenoids from *Tripterygium wilfordii*

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ABSTRACT

An abietane diterpenoid, triptobenzene Y and six sesquiterpene polyol esters, wilforsinines C–H, together with 14 known compounds, have been isolated from the roots of *Tripterygium wilfordii*. The structures of the compounds were elucidated on the basis of spectroscopic analyses. The quinone reductase (QR) induction assay indicated that two compounds showed moderate QR-inducing activities at concentrations of 25 μM and 50 μM, respectively.

1. Introduction

Quinone reductase, a phase II enzyme, plays an important role in anticancer, detoxification pathways and antioxidant defense. Quinone reductase (QR) prevents the toxic effects of quinone compounds by reducing them to hydroquinones, and sustains the capacity of the cells to survive the stress of oxidative metabolites. Some natural products have been found to have activities of inducing quinone reductase (Ma et al., 2009; Colucci et al., 2008).*Tripterygium wilfordii* has been used in the clinical treatment of rheumatoid arthritis and other autoimmune diseases. A series of alkaloids (Wang et al., 2005), diterpenoids (Duan et al., 1999; Li et al., 2010), sesquiterpenes (Itokawa et al., 1994), glycosides (Hwang et al., 1999), and several other components (Yang and Li, 2002) have been isolated from *T. wilfordii*. Some of them have immunosuppressive (Chen et al., 2000), anti-inflammatory (Gong et al., 2008), antitumor (Matsui et al., 2008) and antifertility (Hikim et al., 2000) activities. However, the extract of *T. wilfordii* showed QR induction activity at a concentration of 20 g/mL. Here we report the isolation, structure elucidation and biological activities of an abietane diterpenoid, six sesquiterpene polyol esters (Fig. 1), and 14 known compounds.

2. Results and discussion

Roots of *T. wilfordii* were extracted with EtOH–H_2O (19:1). The concentrated extract was suspended in water and extracted successively with petroleum–ether, CH_2Cl_2, EtOAc and *n*-BuOH. The EtOAc-soluble portion was fractionated by silica gel and reversed phase HPLC to give seven previously unreported compounds (**1**–**7**) and 14 known compounds (**8**–**21**). Their structures were determined by spectroscopic methods.

Compound **1** was obtained as yellow needles, $[\alpha]_D^{25}$ +54.0 (c 0.05, MeOH). Its molecular formula was determined to be $C_{20}H_{28}O_3$ from the positive ion HRESIMS data. Analysis of the IR spectrum indicated presence of hydroxy (3442 cm^{-1}), carbonyl (1704 cm^{-1}) and benzene (1568 cm^{-1}) groups. Comparison of the ^1H and ^{13}C NMR spectroscopic data of **1** (Table 1) with those of triptobenzene B (Takaishi et al., 1997) showed that **1** contained one less methyl and one more aldehyde group. The position of the aldehyde group was determined as C-19 by the evidence of the carbon signal downfield shift from δ_C 28.2 in triptobenzene B to δ_C 207.9 in **1**, and further identified by HMBC correlations of the proton resonances at δ_H 9.86 (H-19) with the carbon resonances at δ_C 52.7 (C-4) and δ_C 77.1 (C-3). The relative configuration of **1** was confirmed by the NOESY correlations of H-20/H-19 and H-3/H-5. Thus, compound **1**, triptobenzene Y, is 3β, 14-dihydroxyabieta-8,11,13-trien-19-al.

Compound **2** was obtained as a colorless amorphous powder, $[\alpha]_D^{25}$ −36.3 (c 0.05, MeOH), and its molecular formula was

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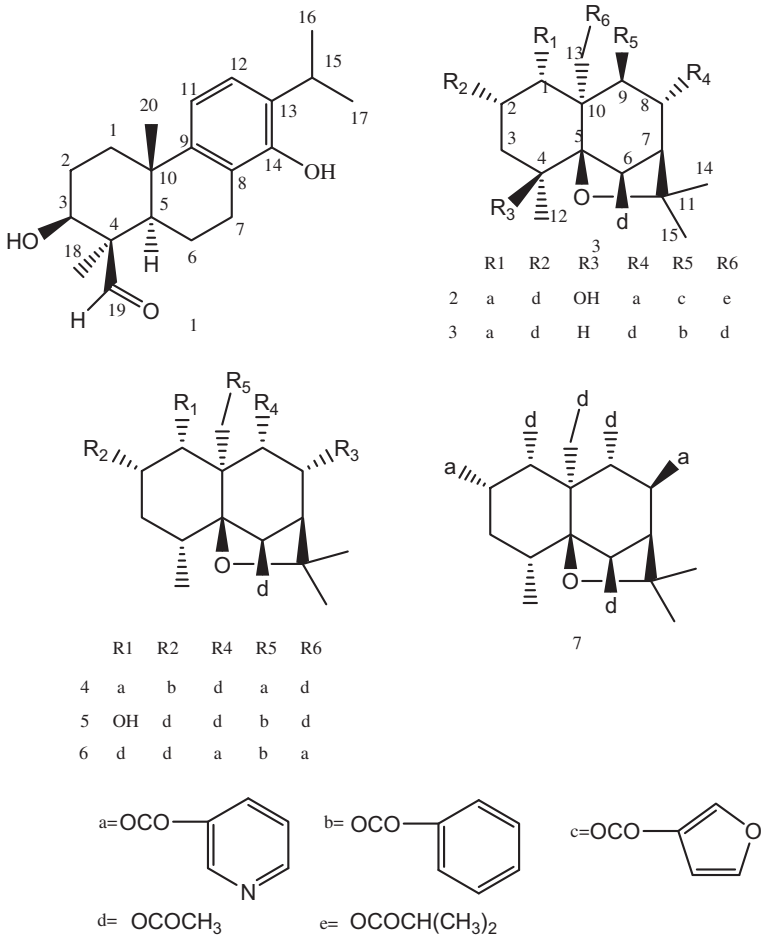

Fig. 1. Structures of compounds **1–7**.

Table 1
^{1}H (500 MHz) and ^{13}C NMR (125 MHz) data of compound 1.[a]

No.	H	C
1	2.35 (*m*); 1.52 (*m*)	37.1
2	2.05 (*m*)	28.9
3	3.27 (*m*)	77.1
4		52.7
5	1.56 (*m*)	51.2
6	2.30 (*m*); 1.95 (*m*)	18.5
7	2.95 (*m*); 2.60 (*m*)	25.1
8		120.7
9		145.8
10		37.5
11	6.85 (*d*, 8.0)	117.0
12	7.02 (*d*, 8.0)	123.6
13		130.5
14		150.2
15	3.10 (*m*)	26.9
16	1.24 (*d*, 7.0)	22.7
17	1.25 (*d*, 7.0)	22.5
18	1.38 (*s*)	19.3
19	9.86 (*s*)	207.9
20	1.13 (*s*)	24.1

[a] Measured in $CDCl_3$.

determined to be $C_{40}H_{44}N_2O_{15}$ by positive ion HRESIMS data. Analysis of the IR spectrum established the presence of hydroxy (3434 cm^{-1}) and carbonyl (1742 cm^{-1}) groups. The NMR spectra displayed the presence of two acetoxy groups, one isobutanoyloxy group, two nicotinoyloxy groups and one 3-furancarbonyloxy group (Wu et al., 2001). The ^{1}H NMR spectrum of **2** indicated presence of three tertiary methyl groups at δ_H 1.54 *s*, 1.62 *s*, and 1.72 *s*. The signals observed at δ_H 5.55 *d* (*J* = 3.0 Hz), 5.72 *d* (*J* = 3.0 Hz), 5.82 *s*, 5.86 *d* (*J* = 3.0 Hz) and 6.47 *s* were assigned to the five protons attached to carbon atoms bearing secondary ester groups, and resonances at δ_H 5.01 *d*, 5.07 *d* (*J* = 13.0 Hz) were assigned to the two protons attached to the carbon atoms bearing primary ester groups. The ^{13}C NMR spectrum of the parent skeleton of **2** (Table 3) showed three methyls, two methylenes, six methines, and four quaternary carbons. These data were suggestive of a β-dihydroagarofuran skeleton (Liu et al., 1991, 1995; Wang et al., 1991; Tu et al., 1992; Wu et al., 2001). HMBC correlations from the skeletal protons to the ester carbonyl groups enabled the nicotinates to be located at C-1 and C-8, the furancarbonyloxy group at C-9, the isobutyrate at C-13 and the acetates at C-2 and C-6. The relative configuration of **2** was assigned by the NOESY correlations of H-13/H-6, H-12/H-6 and H-1/H-2. Thus compound **2**, wilforsinine C, is 2α, 6β-diacetoxy-13-isobutanoyloxy-9β-(3-furancarbonyloxy)-4β-hydroxy-1α,8α-bis(nicotinoyloxy)-β-dih ydroagarofuran.

Compound **3** was obtained as a colorless amorphous powder, $[\alpha]_D^{25}$ +49.0 (c 0.05, MeOH), and its molecular formula was determined to be $C_{36}H_{41}NO_{13}$ by analysis of positive ion HRESIMS data. The IR spectrum indicated the presence of a carbonyl group (1754 cm^{-1}). The NMR spectra of **3** displayed of four acetoxy groups, one nicotinoyloxy group and one benzoyloxy group. Analysis of the NMR spectroscopic data (Tables 2 and 3) suggested that its structure was closely related to that of compound **2**, with the difference being a methine carbon at δ_C 32.7 in **3** instead of the quaternary carbon at δ_C 70.0 in **2**, thus compound **3** also possessed