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Isolation, structure, and bioactivities of abiesadines A–Y, 25 new diterpenes from *Abies georgei* Orr

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ABSTRACT

Twenty-five new (abiesadines A–Y, **1**–**25**) and 29 known (**26**–**54**) diterpenes were isolated from the aerial parts of *Abies georgei*. Abiesadine A (**1**) is a novel 8,14-*seco*-abietane, while abiesadine B (**2**) is a novel 9,10-*seco*-abietane. The structures of the new compounds were established on the basis of spectroscopic data analysis. Manool (**52**) showed the strongest effect against LPS-induced NO production in RAW264.7 macrophages with the IC_{50} value of 11.0 μg/mL. In another anti-inflammatory assay against TNFα-triggered NF-κB activity, (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**54**) exhibited the strongest effect (IC_{50} = 8.7 μg/mL). For antitumor assays, pomiferin A (**26**) and 8,11,13-abietatriene-7α,18-diol (**29**) both showed the most significant activity against LOVO cells (IC_{50} = 9.2 μg/mL). While 7-oxocallitrisic acid (**46**) exhibited significant cytotoxicity against QGY-7703 tumor cells (IC_{50} = 10.2 μg/mL).

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1. Introduction

Abies georgei Orr occurs exclusively in China.[1] Its ethanol extracts showed strong antitumor and anti-inflammatory effects.[2] In a previous study, a novel biflavanol and 22 norditerpenes were reported.[3,4] To continue to explore the chemical constituents of *A. georgei* with novel structures and potent bioactivities, an intensive investigation was carried out, which resulted to the isolation of 25 new (**1**–**25**) and 29 known (**26**–**54**) diterpenes. In this study, we describe the isolation and structural elucidation of new diterpenes from *A. georgei* as well as their inhibitory activity against LPS-induced NO production in RAW264.7 macrophages.

2. Results and discussion

2.1. Identification and structure determination

The $CHCl_3$ and EtOAc-soluble extracts of the aerial parts of *A. georgei* were subjected to column chromatography on silica gel, ODS, and Sephadex LH-20, as well as preparative TLC to yield 25 new (**1**–**25**) and 29 known diterpenes (**26**–**54**) (Fig. 1), among which 46 compounds were abietanes (**1**–**23**, **26**–**48**) and the other 8 were labdanes (**24**, **25**, **49**–**54**).

The molecular formula of compound **1** was assigned as $C_{20}H_{30}O_4$ by its HRESIMS at *m/z* 357.2046 $[M+Na]^+$, indicating six degrees of unsaturation. Absorption of carbonyl (1738 cm^{-1}) and olefinic bond (1684 cm^{-1}) were observed in its IR spectrum. The ^1H and ^{13}C NMR spectra showed 20 carbon signals, including two quaternary and two tertiary methyls [δ_H 0.81 (3H, s, Me-20), 1.15 (3H, s, Me-19), 1.17 (3H, d, *J* = 7.0 Hz, Me-16), 1.19 (3H, d, *J* = 7.0 Hz, Me-17); δ_C 15.3 (q, C-20), 18.0 (q, C-19), 20.5 (q, C-16), 20.6 (q, C-17)], five methines including one aldehyde group [δ_H 9.19 (1H, d, *J* = 1.8 Hz, H-14); δ_C 197. 6 d] and one olefinic bond [δ_H 6.35 (1H, t, *J* = 7.0 Hz, H-12); δ_C 157.6 (d, C-12)], six methylenes, and five quaternary carbons with one ketone, one carbonyl, and one olefinic signals. In the ^1H–^1H COSY spectrum of **1**, correlations of H_2-1/H_2-2/H_2-3, H-5/H_2-6/H_2-7, H-9/H_2-11/H-12, and H_3-16,17/H-15 established four fragments (Fig. 2). In addition, the HMBC correlations originated from four methyls suggested the presence of an abietane structure (Fig. 2). However, according to the unsaturation degrees, compound **1** should only contain two rings. Based on the HMBC correlations of H_2-7 to C-9 (δ_C 65.4 d), the structure of **1** was deduced as a 8,14-*seco*-abietane. This was further confirmed by the HMBC correlations of H-12 to δ_C 197.6 (d) at C-14. In the

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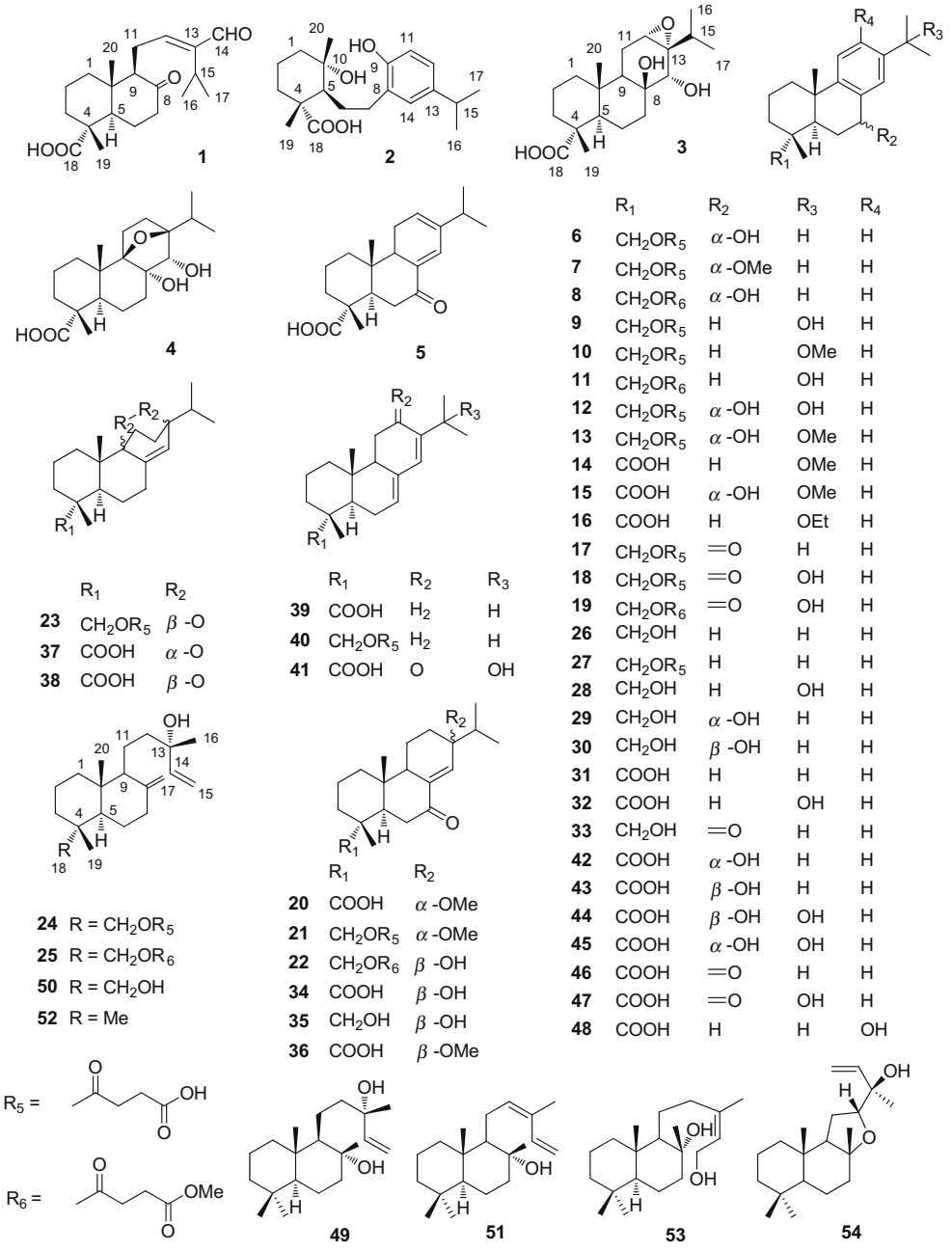

	R_1	R_2	R_3	R_4
6	CH_2OR_5	α-OH	H	H
7	CH_2OR_5	α-OMe	H	H
8	CH_2OR_6	α-OH	H	H
9	CH_2OR_5	H	OH	H
10	CH_2OR_5	H	OMe	H
11	CH_2OR_6	H	OH	H
12	CH_2OR_5	α-OH	OH	H
13	CH_2OR_5	α-OH	OMe	H
14	COOH	H	OMe	H
15	COOH	α-OH	OMe	H
16	COOH	H	OEt	H
17	CH_2OR_5	=O	H	H
18	CH_2OR_5	=O	OH	H
19	CH_2OR_6	=O	OH	H
26	CH_2OH	H	H	H
27	CH_2OR_5	H	H	H
28	CH_2OH	H	OH	H
29	CH_2OH	α-OH	H	H
30	CH_2OH	β-OH	H	H
31	COOH	H	H	H
32	COOH	H	OH	H
33	CH_2OH	=O	H	H
42	COOH	α-OH	H	H
43	COOH	β-OH	H	H
44	COOH	β-OH	OH	H
45	COOH	α-OH	OH	H
46	COOH	=O	H	H
47	COOH	=O	OH	H
48	COOH	H	H	OH

Figure 1. Chemical structures for compounds **1**–**54**.

NOESY spectrum, H_3-20 was correlated to H_3-19/H_2-11, and H-12 to H-14 (Fig. 3). This indicated H-19, 20, and 11 were co-facial, and Δ^{12} an *E*-configuration. On the basis of the above evidences, compound **1** was then identified as (12*E*)-8,14-*oxo*-8,14-secoabiet-12-en-18-oic acid, and named abiesadine A.

Compound **2** was found to possess the molecular formula, $C_{20}H_{30}O_4$, as evidenced by its negative HRESIMS at *m*/*z* 333.2096 $[M-H]^-$. The ^1H and ^{13}C NMR spectra showed 20 carbon signals, including two quaternary methyls, one isopropyl, one ABX benzene ring, and one carboxyl. These signals are characteristic of an abieta-8,11,13-trien-18/19-oic acid. In the HMBC spectrum, H_3-20 was only correlated to δ_C 41.3 (t, C-1), 52.9 (d, C-5), and 80.1 (s, C-10) (Fig. 2). This indicated that a hydroxy group should be located at C-10 position. In addition, the downfield shift of the quaternary carbon at δ_C 153.2 also suggests a hydroxy group at the aromatic moiety. Therefore, compound **2** should be a 9,10-*seco*-9,10-dihydroxyabietane. By detailed analysis for its 2D NMR and the tandem MS spectra (Fig. S13), compound **2** was thus concluded to be 9,10-dihydroxy-9,10-secoabieta-8,11,13-trien-18-oic acid, and named abiesadine B.

Compound **3** was obtained as an amorphous powder. Its molecular formula was established as $C_{20}H_{32}O_5$ on the basis of its negative HRESIMS at *m*/*z* 351.2176 $[M-H]^-$, indicating five degrees of unsaturation. The IR spectrum showed absorption bands characteristic of carboxyl groups (a broad band from 2500 to 3485, 1703 cm^{-1}). The ^1H and ^{13}C NMR spectroscopic data of **3** (Tables 1 and 2) indicated 20 carbon signals including two singlet and two doublet methyls [δ_H 0.86 (3H, d, *J* = 6.9 Hz, Me-16), 0.91 (3H, d, *J* = 6.9 Hz, Me-17), 0.95 (3H, s, Me-20), 1.09 (3H, s, Me-19); δ_C 15.4 (q, Me-20), 16.6 (q, Me-19), 16.9 (q, Me-16), 17.3 (q, Me-17)], six methylenes, three aliphatic sp^3 methines, two oxygenated sp^3 methines [δ_H 3.10 (1H, s, H-14), 3.28 (1H, t, *J* = 1.8 Hz, H-12); δ_C

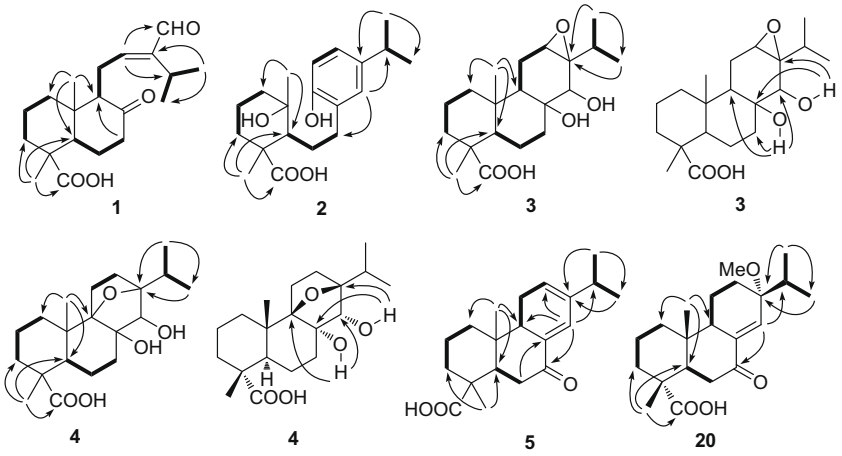

Figure 2. Key $^{1}H–^{1}H$ COSY (bold) and HMBC (arrow, H→C) correlations for compounds **1**–**5**, and **20**.

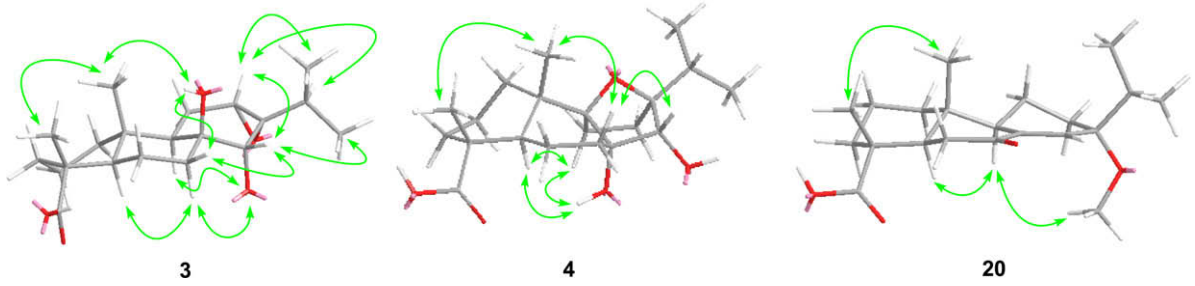

Figure 3. Selected NOESY correlations for compounds **3**, **4**, and **20**.

71.2 (d, C-14), 62.6 (d, C-12)], two aliphatic and two oxygenated sp^3 quaternary carbons (δ_C 71.8 s, 65.2 s), and one carbonyl carbon (δ_C 181.5 s). In the $^{1}H–^{1}H$ COSY spectrum, four fragments were obtained according to the spin systems of H_2-1/H_2-2/H_2-3, H-5/H_2-6/H_2-7, H-9/H_2-11/H-12, and H_3-16,17/H-15. This information, along with the HMBC correlations traced from four methyls (Me-16,17,19,20) suggested the presence of an abietane skeleton (Fig. 2). Taking into consideration the unsaturation degrees, compound **3** should contain another ring obtained by dehydration of two hydroxyls. To further verify this assumption, the deuteriumed solvent of $CDCl_3$ was changed to DMSO-d_6 for another HMBC experiment. Fortunately, the correlations were observed for the proton at 8-OH (δ_H 3.69, 1H, s) to C-7 (δ_C 34.1 t), C-9 (δ_C 41.5 d), C-14 (δ_C 71.5 d), and for the proton at 14-OH (δ_H 3.71, 1H, d, J = 9.6 Hz) to C-13 (δ_C 63.7 s) and C-8 (δ_C 71.0 s) (Fig. 2), which confirmed unambiguously the existence of a three-membered epoxy ring in **3**.

The relative stereochemistry of **3** was established by the NOESY experiment. Based on the NOESY correlations from 8-OH to Me-20/Me-19, to H-7β/H-14/H-12/Me-16/Me-17, to H-15/H-12/Me-16/Me-17, and from 14-OH to H-9/H-7α/H-5 (Fig. 3), the hydroxyls at C-8/12/13/14 were considered as β/α/α/α-orientation, respectively. Therefore, compound **3** was elucidated as 8β,14α-dihydroxy-12,13α-epoxy-abieta-18-oic acid, and named abiesadine C.

Compound **4** exhibited the same molecular formula as **3** based on the negative HRESIMS at m/z 351.2172 $[M-H]^-$. Furthermore, it showed ^{1}H and ^{13}C NMR spectra similar to those of **3**. However, close comparison of the ^{13}C NMR spectroscopic data of **4** and **3** revealed significant differences: four oxygenated sp^3 carbons including two quaternary and two tertiary signals (δ_C 71.0 s, 63.7 s, 71.2 d, and 62.6 d) in **3** were changed to three quaternary and one tertiary ones (δ_C 93.8 s, 88.6 s, 76.0 s, and 76.9 d) in **4**. This indicated that the epoxy three-membered ring of **3** might be altered to an epoxy five-membered ring in **4** through an ether bond between C-9 and C-13. This assumption was supported by the correlation of H_2-11 to H_2-12 in the $^{1}H–^{1}H$ COSY spectrum, and the correlation of H_3-20 to C-9 (δ_C 93.8 s) in the HMBC spectrum (Fig. 2). Furthermore, in its HMBC experiment at DMSO-d_6, the correlations were observed for the proton at 8-OH (δ_H 3.98, 1H, s) to C-7 (δ_C 30.7 t), C-9 (δ_C 91.9 d), C-14 (δ_C 73.5 d), and for the proton at 14-OH (δ_H 5.32, 1H, d, J = 6.0 Hz) to C-8 (δ_C 74.2 s) and C-13 (δ_C 86.5 s) (Fig. 2). This established unequivocally the existence of an epoxy five-membered ring in **4**. Based on the NOESY correlations of H_3-19/H_3-20/H-7β/H-14 and 8-OH/H-5/H-11α (Fig. 3), compound **4** was thus elucidated as 8α,14α-dihydroxy-9,13β-epoxy-abieta-18-oic acid, and named abiesadine D.

Compound **5** had the molecular formula $C_{20}H_{28}O_3$, established from the positive HRESIMS at m/z 339.1950 $[M+Na]^+$, indicating seven unsaturation degrees. The IR spectrum suggested hydroxyls (3433 cm^{-1}), carbonyls (1726, 1672 cm^{-1}) and olefinic bonds (1629, 1596 cm^{-1}) in the structure. Its ^{1}H and ^{13}C NMR spectroscopic data showed 20 carbon signals, including two quaternary methyls, one isopropyl, and one carbonyl moiety, which are characteristic for an abieta-18-oic acid moiety analogous to those presented in **1**–**4**. According to the $^{1}H–^{1}H$ COSY spectrum and the HMBC correlations originating from four methyls and two olefinic protons, the planar structure of **5** was elucidated as shown in Figure 2. In the NOESY spectrum, correlations of H_3-20 to H_3-19 and H_2-11 were found. Accordingly, the relative structure of compound **5** was defined as 7-oxoabieta-8(14),12-dien-18-oic acid, and named abiesadine E.

Compound **6** gave a molecular formula $C_{24}H_{34}O_5$, as established from its positive HRESIMS at m/z 425.2293 $[M+Na]^+$. The ^{1}H and

Table 1
^{1}H NMR spectroscopic data for compounds **1**–**25** (*J* in Hz within parentheses)

No.	**1**[a]	**2**[b]	**3**[c]	**3**[d]	**4**[a]	**4**[d]	**5**[a]
1	1.79 m; 1.40 m	1.94 m; 1.81 m	1.54 m; 0.85 m	1.54 m; 0.79 (dt, 13.2, 3.6)	1.50 m	1.45 m	1.79 (dd, 13.5, 4.0)
2	1.60 m	1.80 m; 1.68 m	1.46 m; 1.39 m	1.40 m; 1.05 m	1.49 m	1.42 m	1.56 m
3	1.84 m; 1.58 m	1.74 m; 1.56 m	1.63 (dt, 13.8, 4.2); 1.46 m	1.58 m; 1.43 m	1.75 m; 1.58 m	1.62 m; 1.47 m	2.40 (dd, 14.7, 5.1); 1.62 m
5	2.48 m	2.53 (dd, 12.0, 2.4)	1.55 m	1.52 m	2.33 m	2.20 (t, 9.0)	2.10 (dd, 14.1, 3.5)
6	1.83 m; 1.75 m	1.53 m	1.55 m; 1.03 m	1.51 m; 0.95 m	1.52 m	1.35 m	2.26 (d, 14.7); 2.48 m
7	2.48 m; 2.30 m	2.84 m; 2.68 (dd, 13.2, 5.4)	1.98 m; 1.27 (br d, 13.8)	1.90 (dt, 13.2, 4.8); 1.32 (br d, 13.2)	1.69 m; 1.52 m	1.50 m; 1.41 m	
9	2.50 m		1.04 m	1.08 m			2.48 m
11	2.69 m; 2.34 m	6.79 (d, 8.4)	1.86 (dd, 15.0, 6.0); 1.81 (dd, 15.0, 2.4)	1.80 (dt, 13.2, 1.8); 1.69 (dd, 13.2, 4.2)	2.09 m; 1.57 m	1.96 (dt, 10.2, 3.0); 1.42 m	2.02 m
12	6.35 (t, 7.0)	6.94 (dd, 8.4, 1.8)	3.28 (t, 1.8)	3.14 br s	1.91 m; 1.18 m	1.81 m; 1.10 m	6.12 m
14	9.19 (d, 1.8)	6.91 (d, 1.8)	3.10 s	3.06 (d, 9.6)	3.15 (d, 1.8)	3.03 (d, 6.0)	6.83 s
15	2.94 (dt, 7.5, 1.5)	2.84 (sept, 7.2)	1.49 m	1.48 m	1.88 m	1.82 m	2.83 (sept, 6.9)
16	1.17 (d, 7.0)	1.22 (d, 7.2)	0.91 (d, 6.9)	0.91 (d, 7.2)	0.96 (d, 6.8)	0.86 (d, 6.6)	1.01 (d, 6.9)
17	1.19 (d, 7.0)	1.22 (d, 7.2)	0.86 (d, 6.9)	0.85 (d, 7.2)	0.94 (d, 6.8)	0.88 (d, 6.6)	1.04 (d, 6.9)
19	1.15 s	1.11 s	1.09 s	1.09 s	1.27 s	1.14 s	1.24 s
20	0.81 s	1.01 s	0.95 s	0.97 s	1.10 s	0.99 s	0.89 s
1′				3.69 s		3.98 s	
2′				3.71 (d, 9.6)		5.32 (d, 6.0)	

No.	**6**[a]	**7**[a]	**8**[e]	**9**[e]	**10**[a]	**11**[f]	**12**[a]
1	1.44 m	2.29 m	2.32 (dt, 12.0, 2.7); 1.32 (dt, 13.2, 3.6)	2.29 m; 1.30 m	2.33 (d, 12.6); 1.36 m	2.30 (dt, 13.2, 2.4); 1.39 (dd, 13.2, 3.6)	2.34 (dt, 12.9, 3.3); 1.38 (dt, 13.2, 3.9)
2	1.83 m; 1.67 m	1.80 m; 1.63 m	1.84 (br d, 13.8); 1.68 m	1.62 m	1.67 m	1.76 m	1.83 (d, 13.8); 1.69 (dt, 14.4, 3.4)
3	1.49 m	1.45 m	1.48 m	1.44 m	2.86 m	1.43 (dd, 10.2, 3.6)	1.52 m
5	2.09 m	1.61 m	2.02 (dt, 12.6, 1.2)	1.59	1.62 (dd, 12.0, 2.4)	1.62 (dd, 12.0, 2.4)	2.08 m
6	1.92 m; 1.85 m	2.27 m; 1.61 m	1.97 (dt, 13.5, 4.2); 1.84 (br d, 13.5)	1.79 m	1.79 m	1.67 m	2.08 (dd, 12.3, 1.2); 1.88 m
7	4.72 (dd, 4.2, 1.8)	4.46 (dd, 4.8, 2.0)	4.72 (dd, 3.6, 1.8)	2.80 m	1.28 m	2.92 (dd, 11.1, 6.6); 2.85 (dd, 11.1, 6.6)	4.75 (dd, 3.9, 1.8)
11	7.19 (d, 8.4)	7.16 (d, 8.4)	7.20 (d, 8.1)	7.18 br s	7.22 (d, 8.4)	7.23 br s	7.25 (d, 8.7)
12	7.08 (dd, 8.4, 1.8)	7.05 (dd, 8.4, 1.8)	7.09 (dd, 8.1, 1.8)	7.18 br s	7.12 (dd, 8.4, 1.8)	7.22 br s	7.35 (dd, 8.4,2.4)
14	7.16 (d, 1.8)	7.23 (d, 1.8)	7.16 (d, 1.8)	7.11 s	7.02 (d, 1.8)	7.16 br s	7.41 (d, 2.1)
15	2.84 m	2.82 m	2.84 (sept, 7.2)				
16	1.21 (d, 7.2)	1.21 s	1.22 (d, 7.2)	1.48 s	1.47 s	1.56 s	1.50 s
17	1.21 (d, 7.2)	1.20 s	1.22 (d, 7.2)	1.48 s	1.47 s	1.56 s	1.50 s
18	3.99 (d, 10.8); 3.72 (d, 10.8)	4.11 (d, 11.1); 3.66 (d, 11.1)	4.02 (d, 10.8); 3.72 (d, 10.8)	4.01 (d, 9.6); 3.72 (d, 9.6)	4.02 (d, 10.8); 3.73 (d, 10.8)	3.99 (d, 10.8); 3.75 (d, 10.8)	4.01 (d, 11.1); 3.73 (d, 10.8)
19	0.97 s	0.98 s	0.96 s	0.95 s	0.96 s	0.94 s	0.97 s
20	1.16 s	1.26 s	1.16 s	1.20 s	1.22 s	1.22 s	1.17 s
2′	2.56 m	2.58 m	2.60 m	2.56 m	2.58 m	2.61 br s	2.58 m
3′	2.45 m	2.55 m	2.61 m	2.57 m	2.58 m	2.61 br s	2.59 m
OMe		3.47 s	3.59 s		3.02 s	3.62 s	

No.	**13**[a]	**14**[a]	**15**[a]	**16**[a]	**17**[a]	**18**[a]
1	2.35 (dt, 12.6, 3.3); 1.39 (dt, 12.6, 3.3)	2.33 (d, 12.2); 1.44 m	2.33 (br d, 12.6); 1.47 m	2.33 (d, 12.6)	2.41 m; 1.49 m	2.41 (d, 12.9); 1.55 (dt, 12.9, 3.0)
2	1.87 m; 1.68 m	1.82 m; 1.68 m	1.80 m; 1.71 m	1.67 m; 1.57 m	1.85 m; 1.72 m	1.90 m; 1.75 m
3	1.53 m	1.81 m; 1.59 m	1.88 (dd, 13.2, 3.3); 1.67 m	1.80 m; 1.59 m	1.48 m	1.49 m
5	2.09 (dd, 12.3, 1.2)	2.19 (dd, 12.2, 2.4)	2.49 (dd, 12.9, 2.1)	2.19 (dd, 12.6, 2.1)	2.17 (dd, 13.8, 4.2)	2.18 (dd, 14.1, 3.9)
6	1.99 (dt, 13.5, 4.2); 1.87 (br d, 13.5)	1.84 m; 1.57 m	2.11 (dt, 13.2, 4.8); 1.65 m	1.85 m; 1.56 m	2.64 m	2.74 (dt, 18.0, 13.8); 2.64 (18.0, 4.2)
7	4.75 (dd, 3.3, 1.5)	2.86 m	4.72 (dd, 4.2, 1.2)	2.87 m		
11	7.28 br s	7.21 (d, 8.4)	7.23 (d, 8.4)	7.21 (d, 8.4)	7.39 (d, 8.4)	7.43 (d, 8.4)
12	7.28 br s	7.11 (dd, 8.4, 2.4)	7.24 (dd, 8.4, 1.8)	7.12 (dd, 8.4, 2.1)	7.47 (dd, 8.4, 2.1)	7.72 (dd, 8.4, 1.8)
14	7.33 br s	7.01 (d, 2.4)	7.33 (d, 1.8)	7.01 (d, 2.1)	7.79 (d, 2.1)	8.05 (d, 1.8)
15					2.91 (sept, 7.2)	
16	1.50 s	1.46 s	1.49 s	1.46 s	1.24 (d, 7.2)	1.52 s
17	1.50 s	1.46 s	1.49 s	1.46 s	1.24 (d, 7.2)	1.52 s
18	4.01 (d, 11.1); 3.73 (d, 11.1)				3.91 (d, 11.4); 3.74 (d, 11.4)	3.93 (d, 11.4); 3.75 (d, 11.4)

(*continued on next page*)

Table 1 (*continued*)

No.	**13**[a]	**14**[a]	**15**[a]	**16**[a]	**17**[a]	**18**[a]
19	0.98 s	1.24 s	1.25 s	1.24 s	1.05 s	1.06 s
20	1.18 s	1.20 s	1.15 s	1.20 s	1.27 s	1.28 s
1′				3.19 (quart, 6.9)		
2′	2.58 m			1.10 (t, 6.9)	2.44 m	2.54 m
3′	2.58 m				2.43 m	2.52 m
OMe	3.04 s	3.02 s	3.04 s			

No.	**19**[b]	**20**[a]	**21**[a]	**22**[b]	**23**[a]	**24**[b]	**25**[b]
1	2.36 (dt, 13.2, 3.0); 1.54 (dd, 13.2, 3.0)	1.80 m; 1.22 m	1.80 (d, 13.5); 1.18 m	1.82 m; 1.11 m	1.57 m	1.77 (br d, 13.2) 1.03 (dt, 13.2, 4.8)	1.77 (d, 12.2) 1.01(dt, 12.2, 4.2)
2	1.77 m	1.59 m	1.53-1.61 m	1.59 m; 1.12 m	1.51 m; 1.02 m	1.54 m	1.53 m
3	1.47 m	1.76 m	1.44 m	1.42 m; 1.39 m	1.42 m	1.35 m	1.34 m
5	2.18 (dd, 12.0, 6.0)	2.40 m	1.88 (dd, 13.5, 5.7)	1.80 m	1.54 m	1.34 m	1.33 m
6	2.65 m	2.36 m	2.54 (dd, 13.5, 5.4); 2.40 (d, 13.5)	2.50 (dd, 18.6, 5.4); 2.32 (dd, 18.6, 13.8)	2.23 m; 1.52 m	1.57 m; 1.34 m	1.56 m; 1.34 m
7					1.92 m; 1.46 m	2.35 (d, 13.2); 1.95 m	2.35 (d, 11.4); 1.93 m
9		2.22 m	2.08 (t, 6.9)	2.03 m		1.63 (d, 10.2)	1.58 m
11	3.37 (d, 8.4)	1.83 m; 1.48 m	1.69 m; 1.73 m	1.76 m; 1.48 m	1.55 m	1.34 m	1.35 m
12	7.73 (dd, 8.4, 2.1)	1.79 m	1.71 m; 1.48 m	1.73 m	2.72 m; 2.38 m	1.72 (dd, 13.2, 4.2); 1.27 m	1.72 (dd, 12.2, 4.2); 1.25 m
14	8.06 (d, 2.1)	6.69 (d, 3.0)	6.72 m	6.75 (t, 2.1)	6.15 (t, 2.1)	5.91 (dd, 17.6, 10.8)	5.90 (dd, 17.4, 10.8)
15		1.84 m	2.08 (t, 6.9)	1.79 m	1.79 (sept, 6.9)	5.19 (d, 17.6); 5.04 (d, 10.8)	5.19 (dd, 17.4, 1.2); 5.04 (dd, 10.8, 1.2)
16	1.58 s	0.92 (d, 6.6)	0.89 (d, 6.9)	0.97 (d, 7.2)	0.94 (d, 6.9)	1.27 s	1.26 s
17	1.59 s	0.90 (d, 6.6)	0.79 (d, 6.9)	0.87 (d, 7.2)	0.96 (d, 6.9)	4.82 s; 4.52 s	4.81 s; 4.52 s
18	3.87 (d, 10.8); 3.77 (d, 10.8)		3.87 (d, 11.1); 3.65 (d, 11.1)	3.82 (d, 11.4); 3.68 (d, 11.4)	3.88 (d, 10.8); 3.62 (d, 10.8)	3.90 (d, 11.1); 3.65 (d, 11.1)	3.87 (d, 10.8); 3.66 (d, 10.8)
19	1.02 s	1.20 s	0.95 s	0.94 s	0.99 s	0.81 s	0.81 s
20	1.26 s	0.87 s	0.89 s	0.87 s	1.11 s	0.71 s	0.70 s
2′	2.59 br s		2.59 m	2.63 m	2.56 m	2.64 m	2.64 m
3′	2.59 br s		2.56 m	2.65 m	2.47 m	2.64 m	2.64 m
OMe	3.60 s	3.10 s	3.18 s	3.67 s			3.69 s

[a] Measured at 300 MHz in CD_3OD.
[b] Measured at 600 MHz in $CDCl_3$.
[c] Measured at 600 MHz in $CDCl_3$ + CD_3OD.
[d] Measured at 600 MHz in DMSO-d_6.
[e] Measured at 600 MHz in CD_3OD.
[f] Measured at 300 MHz in $CDCl_3$

^{13}C NMR spectroscopic data were similar to those of **29**, with the only difference being the presence of an additional succinic acid [δ_H 2.45 (2H, m, H-3′), 2.56 (2H, m, H-2′); δ_C 175.5 (s, C-1′), 31.7 (t, C-2′), 33.0 (t, C-3′), 180.0 (s, C-4′)]. Compared to **29**, C-18 was shifted downfield by 1.5, which supposed the connection of succinic acid to C-18 carbon. The assumption was confirmed by the HMBC correlations of H_2-18 (3.99, 3.72 each for 1H) to the carbonyl group (δ_C 175.5) at C-1′ of the succinic acid. Thus, compound **6** was determined as 8,11,13-abietatriene-7α-hydroxy-18-succinic acid, and named abiesadine F.

Compound **7** presented a molecular formula of $C_{25}H_{36}O_5$ by negative HRESIMS at *m/z* 415.2571 $[M-H]^-$. The ^1H and ^{13}C NMR spectra consisted of signals similar to those of **29** except for an additional methoxyl [δ_H 3.47 (3H, s); δ_C 55.9 (q)]. The downfield shift of C-7 in **7** from δ_C 68.7 to 80.4 when compared to **29** suggested the attachment of a methoxy group to the C-7 carbon, which was confirmed by the HMBC correlation of the methoxyl (δ_H 3.47) to C-7 at δ_C 80.4. Consequently, compound **7** was assigned as 8,11,13-abietatriene-7α-methoxy-18-succinic acid, and named abiesadine G.

Compound **8** shared the same molecular formula $C_{25}H_{36}O_5$ as **7**. In addition, they shared almost the same IR, ^1H and ^{13}C NMR spectroscopic data. However, a close inspection of their ^{13}C NMR spectroscopic data revealed significant differences: the oxygenated methine at C-7 and the carbonyl group in **8** were shifted upfield by 11.8 and 4.4, respectively. This indicated that the methoxy unit should be located at C-4′ carbon of the succinic acid in **8** instead of C-7 position of **7**, which was supported by the HMBC correlation of the methoxyl (δ_H 3.59) to the carboxyl (δ_C 174.8) of the succinic acid moiety. Thus, compound **8** was characterized as methyl 8,11,13-abietatriene-7α-hydroxyl-18-succinate, and named abiesadine H.

Compound **9** possessed a molecular formula $C_{24}H_{34}O_6$ from its HRESIMS at *m/z* 425.2312 $[M+Na]^+$, and exhibited ^1H and ^{13}C NMR spectra very similar to those of **28** except for an additional succinic acid [δ_H 2.56 (2H, m, H-2′), 2.57 (2H, m, H-3′); δ_C 174.2 (s, C-1′), 30.4 (t, C-2′), 30.3 (t, C-3′), 174.3 (s, C-4′)]. Close inspection of the ^{13}C NMR spectroscopic data of **9** exhibited the difference from those of **28**: the oxygenated methylene at C-18 position in **9** was shifted downfield by 1.7, which suggested the connection of the succinic acid moiety to C-18 carbon. Further evidence was found in the HMBC correlation of H_2-14 (4.01, 3.72 each for 1H) to C-1′ at δ_C 174.3. Thus, compound **9** was identified to be 8,11,13-abietatriene-15-hydroxy-18-succinic acid, and named abiesadine I.

Compound **10** showed a molecular ion peak at *m/z* 439.2459 $[M+Na]^+$ in its positive HRESIMS, corresponding to the molecular formula of $C_{25}H_{36}O_5$. Its ^1H and ^{13}C NMR spectroscopic data were very similar to those of **9**, except for the presence of an additional methoxy group [δ_H 3.02 (3H, s); δ_C 50.8 (q)] at C-15. In the HMBC

Table 2
^{13}C NMR spectroscopic data for compounds **1**–**25**, **28**, **29**, **32**, **35**, **36**, **38**, and **49**

No.	**1**[a]	**2**[b]	**3**[c]	**3**[d]	**4**[a]	**4**[d]	**5**[a]	**6**[a]	**7**[a]	**8**[e]	**9**[e]	**10**[a]	**11**[f]	**12**[a]	**13**[a]	**14**[a]	**15**[a]
1	39.9 t	41.3 t	38.5 t	38.7 t	39.3 t	37.8 t	39.1 t	39.4 t	39.6 t	39.4 t	39.6 t	39.6 t	38.2 t	37.8 t	39.2 t	39.5 t	38.5 t
2	19.3 t	18.0 t	17.3 t	17.2 t	19.4 t	18.1 t	19.1 t	19.9 t	19.4 t	19.6 t	19.5 t	19.6 t	18.9 t	18.1 t	19.6 t	19.9 t	19.2 t
3	38.6 t	37.0 t	36.4 t	36.3 t	38.7 t	36.9 t	38.6 t	36.8 t	36.5 t	36.7 t	36.7 t	36.6 t	35.5 t	35.2 t	36.7 t	38.2 t	37.2 t
4	49.3 s	48.8 s	46.8 s	46.3 s	47.7 s	45.7 s	47.4 s	37.4 s	37.9 s	37.5 s	37.9 s	38.0 s	36.8 s	36.0 s	37.5 s	48.2 s	47.7 s
5	49.9 d	52.9 d	49.2 d	48.9 d	39.7 d	37.9 d	45.0 d	40.2 d	43.8 d	40.1 d	45.9 d	45.8 d	44.2 d	38.6 d	40.1 d	46.7 d	40.4 d
6	27.0 t	25.6 t	19.9 t	20.0 t	20.1 t	18.8 t	38.4 t	29.9 t	25.7 t	30.1 t	20.1 t	20.1 t	18.5 t	28.4 t	29.8 t	22.8 t	31.8 t
7	43.0 t	34.7 t	34.4 t	34.1 t	32.0 t	30.7 t	202.0 s	68.7 d	80.4 d	68.6 d	31.4 t	31.4 t	30.3 t	67.3 d	68.7 d	31.4 t	68.1 d
8	213.3 s	135.4 s	71.8 s	71.0 s	76.0 s	74.2 s	135.1 s	136.9 s	136.2 s	136.9 s	139.0 s	135.8 s	134.7 s	135.1 s	136.9 s	136.0 s	136.6 s
9	65.4 d	153.2 s	41.5 d	41.5 d	93.8 s	91.9 s	50.1 d	148.4 s	148.8 s	148.4 s	148.9 s	149.6 s	148.1 s	147.5 s	149.6 s	149.9 s	148.9 s
10	43.1 s	80.1 s	35.5 s	35.3 s	38.3 s	36.5 s	35.7 s	38.9 s	39.0 s	38.9 s	38.5 s	38.7 s	37.4 s	37.4 s	39.0 s	38.3 s	38.1 s
11	23.1 t	123.5 d	20.6 t	20.7 t	27.5 t	26.0 t	27.4 t	125.0 d	125.3 d	125.3 d	125.0 d	125.4 d	124.3 d	123.6 d	125.4 d	125.3 d	124.7 d
12	157.6 d	124.5 d	62.6 d	59.9 d	25.4 t	23.9 t	134.6 d	127.2 d	126.7 d	127.2 d	123.1 d	124.3 d	121.9 d	124.1 d	126.7 d	124.3 d	126.3 d
13	148.6 s	143.6 s	65.2 s	63.7 s	88.6 s	86.5 s	142.6 s	147.2 s	147.2 s	147.3 s	147.4 s	143.4 s	145.9 s	146.6 s	144.0 s	143.3 s	143.5 s
14	197.6 d	127.5 d	71.2 d	71.5 d	76.9 d	75.3 d	143.4 d	129.4 d	126.8 d	129.3 d	125.9 d	127.3 d	124.9 d	126.1 d	129.0 d	127.4 d	128.5 d
15	27.6 d	33.4 d	34.0 d	33.8 d	34.0 d	32.2 d	27.4 d	34.9 d	35.0 d	34.9 d	72.7 s	78.1 s	72.2 s	71.3 s	78.1 s	78.1 s	77.8 s
16	20.5 q	24.2 q	16.9 q	17.7 q	17.8 q	17.4 q	21.9 q	24.5 q	24.4 q	24.4 q	31.9 q	28.2 q	31.6 q	30.3 q	28.2 q	28.2 q	28.0 q
17	20.6 q	24.2 q	17.3 q	17.7 q	18.0 q	17.6 q	22.3 q	24.5 q	24.4 q	24.4 q	31.9 q	28.2 q	31.6 q	30.3 q	28.2 q	28.3 q	28.1 q
18	185.4 s	182.8 s	181.5 s	179.8 s	182.3 s	179.4 s	183.8 s	73.8 t	72.9 t	73.7 t	73.6 t	73.6 t	72.7 t	72.3 t	73.7 t	184.8 s	181.9 s
19	18.0 q	16.1 q	16.6 q	17.0 q	18.5 q	17.9 q	17.7 q	17.9 q	17.9 q	17.8 q	17.9 q	17.8 q	17.4 q	16.3 q	17.7 q	17.6 q	16.9 q
20	15.3 q	20.7 q	15.4 q	15.7 q	18.0 q	17.4 q	14.7 q	24.9 q	25.9 q	24.9 q	25.7 q	25.7 q	25.3 q	23.3 q	24.8 q	25.5 q	24.5 q
1′								175.5 s	175.0 s	174.2 s	174.2 s	174.2 s	172.3 s	172.9 s	174.4 s		
2′								31.7 t	31.4 t	29.7 t	30.4 t	29.8 t	28.9 t	28.7 t	29.8 t		
3′								33.0 t	31.5 t	29.9 t	30.3 t	30.1 t	29.2 t	28.4 t	30.2 t		
4′								180.0 s	179.2 s	174.8 s	174.3 s	176.0 s	172.7 s	174.8 s	180.3 s		
OMe									55.9 q	52.2 q		50.8 q	51.7 q		50.8 q	50.8 q	50.9 d

No.	**16**[a]	**17**[a]	**18**[a]	**19**[b]	**20**[a]	**21**[a]	**22**[b]	**23**[a]	**24**[b]	**25**[b]	**28**[a]	**29**[a]	**32**[a]	**35**[a]	**36**[a]	**38**[a]	**49**[a]
1	39.5 t	38.6 t	38.6 t	37.3 t	39.0 t	39.2 t	38.3 t	35.2 t	38.5 t	38.5 t	39.8 t	39.5 t	39.6 t	37.9 t	39.4 t	35.0 t	41.1 t
2	19.9 t	19.1 t	19.1 t	18.0 t	19.1 t	18.9 t	17.8 t	18.5 t	18.5 t	18.5 t	19.8 t	19.7 t	20.1 t	19.0 t	19.2 t	18.9 t	20.5 t
3	38.3 t	36.4 t	36.4 t	35.2 t	38.5 t	36.7 t	35.6 t	37.2 t	36.0 t	36.0 t	36.2 t	36.2 t	38.5 t	36.4 t	38.6 t	38.8 t	43.2 t
4	49.3 s	37.8 s	37.8 s	37.6 s	47.9 s	37.8 s	36.7 s	38.6 s	37.0 s	37.0 s	38.9 s	38.5 s	48.5 s	38.7 s	48.0 s	48.2 s	34.2 s
5	46.7 d	45.0 d	44.9 d	43.2 d	46.2 d	45.1 d	43.8 d	40.5 d	49.3 d	49.5 d	44.9 d	40.0 d	22.9 t	43.7 d	46.1 d	41.8 d	57.5 d
6	22.8 t	37.0 t	37.0 t	35.9 t	39.5 t	38.2 t	37.2 t	24.5 t	24.3 t	24.3 t	19.9 t	29.7 t	46.9 d	39.8 t	40.1 t	21.7 t	21.5 t
7	31.4 t	201.4 s	201.2 s	198.7 s	201.8 s	201.7 s	199.8 s	28.9 t	37.9 t	38.0 t	31.2 t	68.7 d	31.5 t	202.8 s	202.2 s	29.1 t	45.0 t
8	136.0 s	131.6 s	131.4 s	130.4 s	142.0 s	142.3 s	138.5 s	145.6 s	148.1 s	148.0 s	135.7 s	137.1 s	135.8 s	139.6 s	142.7 s	145.8 s	75.2 s
9	149.8 s	155.3 s	155.7 s	154.1 s	52.4 d	52.4 d	51.5 d	83.6 s	57.2 d	57.3 d	149.2 s	148.5 s	149.4 s	53.1 d	50.5 d	83.7 s	62.9 d
10	38.1 s	38.9 s	38.9 s	36.7 s	36.8 s	37.1 s	35.8 s	40.1 s	39.7 s	39.7 s	38.4 s	38.8 s	38.1 s	36.8 s	36.8 s	39.8 s	40.5 s
11	125.2 d	125.2 d	125.0 d	123.7 d	22.0 t	19.6 t	18.4 t	20.0 t	17.7 t	17.7 t	125.0 d	127.1 d	125.9 d	19.5 t	19.6 t	24.6 t	19.5 t
12	124.2 d	134.2 d	132.2 d	130.5 d	26.8 t	27.8 t	29.5 t	26.4 t	41.1 t	41.4 t	123.0 d	125.2 d	124.9 d	30.6 t	27.9 t	26.4 t	46.4 t
13	144.1 s	148.1 s	149.1 s	147.2 s	78.9 s	77.0 s	71.8 s	81.2 s	73.8 s	73.4 s	147.3 s	147.2 s	147.3 s	72.6 s	77.1 s	81.1 s	74.6 s
14	127.2 d	125.6 d	124.1 d	123.1 d	142.0 d	139.9 d	139.7 d	127.5 d	145.3 d	145.3 d	125.9 d	129.2 d	123.0 d	141.7 d	139.9 d	127.5 d	146.5 d
15	77.8 s	34.8 d	72.6 s	72.2 s	37.8 d	34.1 d	37.8 d	33.5 d	111.5 t	111.5 t	72.8 s	34.9 d	72.8 s	39.1 d	34.2 d	33.4 d	111.9 t
16	28.7 q	24.2 q	31.7 q	31.6 q	17.2 q	16.3 q	16.2 q	17.5 q	27.3 q	27.7 q	31.9 q	24.4 q	31.9 q	16.6 q	17.2 q	17.5 q	28.2 q
17	28.8 q	24.2 q	31.7 q	31.6 q	17.8 q	17.7 q	17.4 q	17.6 q	106.8 t	106.8 t	31.9 q	24.5 q	31.9 q	17.7 q	17.8 q	17.6 q	24.0 q
18	185.0 s	72.9 t	72.9 t	71.8 t	183.9 s	72.9 t	72.0 t	73.3 t	73.1 t	73.2 t	71.9 t	72.3 t	183.8 s	71.1 t	184.5 s	183.1 s	21.9 q
19	17.6 q	17.6 q	17.5 q	17.2 q	17.4 q	17.4 q	17.1 q	18.9 q	17.5 q	17.4 q	18.0 q	17.7 q	18.0 q	17.6 q	16.3 q	18.0 q	33.9 d
20	25.5 q	24.1 q	24.1 q	23.8 q	14.5 q	14.7 q	14.5 q	18.6 q	14.8 q	14.8 q	25.8 q	24.9 q	25.6 q	15.1 q	14.6 q	19.0 q	16.0 q
1′	59.1 t	174.8 s	174.2 s	172.1 s		174.0 s	172.1 s	175.0 s	172.5 s	172.1 s							
2′	16.1 q	31.6 t	30.1 t	28.8 t		30.2 t	28.9 t	31.7 t	29.4 t	29.0 t							
3′		31.0 t	30.2 t	29.1 t		29.8 t	29.2 t	32.8 t	29.5 t	29.3 t							
4′		179.0 s	176.1 s	172.6 s		175.9 s	172.7 s	179.4 s	176.7 s	172.6 s							
OMe				51.7 q	50.6 q	50.5 q	51.8 q			51.7 q					53.1 q		

[a] Measured at 75 MHz in CD_3OD.
[b] Measured at 150 MHz in $CDCl_3$.
[c] Measured at 150 MHz in $CDCl_3$ + CD_3OD.
[d] Measured at 150 MHz in DMSO-d_6.
[e] Measured at 150 MHz in CD_3OD.
[f] Measured at 75 MHz in $CDCl_3$.

spectrum, the long-range correlation of 15-OMe to C-15 (δ_C 78.1) was found. Therefore, compound **10** was concluded to be 8,11,13-abietatriene-15-methoxy-18-succinic acid, and named abiesadine J.

Compound **11** had the same molecular formula as **10**. In addition, the two compounds shared almost the same IR, ^{1}H, and ^{13}C NMR spectroscopic data. However, close inspection of their ^{13}C NMR spectroscopic data revealed significant differences: the oxygenated methine at C-15 and the carbonyl group at C-4′ in **11** were shifted upfield by 5.9 and 3.7, respectively. This indicated that the methoxy group should locate at C-4′ carbon of the succinic acid in **11** instead of C-15 position in **10**. Accordingly, compound **11** was then elucidated as methyl 8,11,13-abietatriene-15-hydroxyl-18-succinate, and named abiesadine K.

Compound **12** was assigned the molecular formula $C_{24}H_{34}O_6$, by negative HRESIMS at *m/z* 417.2278 $[M-H]^-$. Its NMR spectroscopic data were similar to those of **6**, except for the presence of a hydroxy group at C-15 position. By detailed analysis of the 2D NMR spectroscopic data, compound **12** was determined as 8,11,13-abietatriene-7α,15-dihydroxy-18-succinic acid, and named abiesadine L.

The molecular formula of compound **13**, $C_{25}H_{36}O_6$, was established from the negative HRESIMS at *m/z* 431.2435 $[M-H]^-$. Its ^{1}H and ^{13}C NMR spectroscopic data were very similar to those of

12, except for an additional methoxy group as indicated by a ^{1}H NMR resonance at δ_H 3.04 (3H, s) and the corresponding ^{13}C NMR resonance at δ_C 50.8 (q). The methoxy substituent was deduced to be connected to position C-15 on the basis of the HMBC correlation from 15-OMe to C-15 (δ_C 78.1) carbon. Accordingly, **13** was elucidated as 8,11,13-abietatriene-7α-hydroxy-15-methoxy-18-succinic acid, and named abiesadine M.

Compound **14** had the molecular formula $C_{21}H_{30}O_3$ as established from its negative HRESIMS (*m/z* 329.2116 [M−H]$^-$). Its ^{1}H and ^{13}C NMR spectroscopic data were very similar to those of **32**, except for an additional methoxy group [δ_H 3.02 (3H, s); δ_C 50.8 (q)]. The C-15 downfield shift from δ_C 72.8 to 78.1 when compared with **32** indicated the attachment of the methoxy substituent to the C-15 carbon. Therefore, **14** was determined as 8,11,13-abietatriene-15-methoxy-18-oic acid, and named abiesadine N.

Compound **15** exhibited a [M−H]$^-$ ion peak at *m/z* 345.2064 in the positive HRESIMS, corresponding to the molecular formula, $C_{21}H_{30}O_4$. The ^{1}H and ^{13}C NMR spectroscopic data of **15** were very similar to those of **14** except for an additional hydroxy substituent at C-7. This was confirmed by the correlations of H-5/H-6a, H-6a/H-6b, and H-6b/H-7 in the ^{1}H–^{1}H COSY experiment, and H-7 to C-14 in the HMBC spectrum. According to the small coupling constant of H-7 (dd, *J* = 4.2, 1.2 Hz), 7-OH was determined as α-orientated.[3] Therefore, compound **15** was assigned as 8,11,13-abietatriene-7α-hydroxy-15-methoxy-18-oic acid, named abiesadine O.

Compound **16** was assigned the molecular formula $C_{22}H_{32}O_3$ from its positive HRESIMS (*m/z* 367.2304 [M+Na]$^+$). The ^{13}C NMR spectroscopic data were similar to those of **32** except that the hydroxy moiety at C-15 in **32** was replaced by an ethoxy group [δ_H 3.19 (2H, quart, *J* = 6.9 Hz), 1.10 (3H, t, *J* = 6.9 Hz); δ_C 59.1 (t), 16.1 (q)] in **16**. According to the HMBC correlations of H_2-1′ at δ_H 3.19 to the C-15 at δ_C 77.8, compound **16** was then determined to be 8,11,13-abietatriene-15-ethoxy-18-oic acid, and named abiesadine P. It may be an artifact during the isolation procedures since 80% EtOH was used as solvent for extraction.

Compound **17** exhibited a [M−H]$^-$ ion peak at *m/z* 399.2128 in the negative HRESIMS, corresponding to the molecular formula $C_{24}H_{32}O_5$. Comparison of its ^{1}H and ^{13}C NMR spectroscopic data with those of **33** revealed many similarities except for an additional succinic acid [δ_H 2.44 (2H, m, H-2′), 2.43 (2H, m, H-3′); δ_C 174.8 (s, C-1′), 31.6 (t, C-2′), 31.0 (t, C-3′), 178.2 (s, C-4′)]. Observation of the correlation from H_2-18 at δ_H 3.91 and 3.74 (each for 1H, d, *J* = 11.4 Hz) to C-1′ at δ_C 174.8 permitted the succinic acid moiety to be placed at C-18 carbon. Thus compound **17** was deduced as 7-*oxo*-8,11,13-abietatriene-18-succinic acid, and named abiesadine Q.

Compound **18** was assigned the molecular formula $C_{24}H_{32}O_6$, by negative HRESIMS at *m/z* 415.2133 [M−H]$^-$. The ^{1}H and ^{13}C NMR spectroscopic data were similar to those of **17** in addition to a hydroxy group at C-15 carbon. By detailed analysis of its HSQC, ^{1}H–^{1}H COSY, HMBC, and NOESY spectra, compound **18** was consequently determined to be 7-*oxo*-8,11,13-abietatriene-15-hydroxy-18-succinic acid, named abiesadine R.

Compound **19** had a molecular formula of $C_{25}H_{34}O_6$ as suggested by its positive HRESIMS at *m/z* 453.2286 [M+Na]$^+$. Close comparison of the ^{13}C NMR spectrum of compound **19** and that of **18** showed a general similarity except that a hydroxy group in **18** was replaced by a methoxy moiety [δ_H 3.60 (3H, s); δ_C 51.7 (q)]. Since the methoxy group at δ_H 3.60 was correlated to δ_C 172.6 in the HMBC spectrum, the methoxyl was attached to C-4′ position of the succinic acid. On the basis of the above evidence, compound **19** was assigned as methyl 7-*oxo*-8,11,13-abietatriene-15-hydroxy-18-succinate, and named abiesadine S.

Compound **20** gave the same molecular formula $C_{21}H_{32}O_4$ as **36** from its negative HRESIMS at *m/z* 347.2220 [M−H]$^-$. Furthermore, the two compounds exhibited very similar ^{1}H and ^{13}C NMR spectra. According to HMQC, ^{1}H–^{1}H COSY, and HMBC NMR spectroscopic data, the planar structure was established the same as that of **36**. In the NOESY spectrum, the correlations were found of 13-OMe at δ_H 3.10 to H-9 at δ_H 2.22, and H-9 to H-5 at δ_H 2.40. Furthermore, another correlation of Me-19 to Me-20 was also found. Based on the above evidences, compound **20** was determined to be 13α-methoxy-7-*oxo*-8(14)-abieten-18-oic acid, and named abiesadine T.

The molecular formula of compound **21**, $C_{25}H_{38}O_6$, was deduced by its positive HRESIMS at *m/z* 457.2509 [M+Na]$^+$. Its IR, ^{1}H, and ^{13}C NMR spectroscopic data were very similar to those of **20** except that a succinic acid moiety [δ_H 2.56 (2H, m, H-3′), 2.59 (2H, m, H-2′); δ_C 174.0 (s, C-1′), 30.2 (t, C-2′), 29.8 (t, C-3′), 175.9 (s, C-4′)] was located at C-18 in **21**, instead of a carboxyl group in **20**. Therefore, **21** was concluded to be 7-*oxo*-13α-methoxy-8,11,13-abietatriene-18-succinic acid, and named abiesadine U.

Compound **22** gave its molecular formula $C_{25}H_{38}O_6$ as deduced by the HRESIMS (*m/z* 457.2565 [M+Na]$^+$). The ^{1}H and ^{13}C NMR spectra were closely similar to those of **35** except for an additional methoxy group [δ_H 3.67 (3H, s); δ_C 51.8 (q)] and a succinic acid moiety [δ_H 2.63 (2H, m, H-2′), 2.65 (2H, m, H-3′); δ_C 172.1 (s, C-1′), 28.9 (t, C-2′), 29.2 (t, C-3′), 172.7 (s, C-4′)]. In the HMBC, correlations were found for H_2-18 to C-1′ at δ_C 172.1, and for the methoxyl to C-4′ at δ_C 172.7. As such, compound **22** was determined to be methyl 7-*oxo*-13β-hydroxy-8,11,13-abietatriene-18-succinate, and named abiesadine V.

Compound **23** was established its molecular formula, $C_{24}H_{38}O_6$, as deduced by its positive HRESIMS at *m/z* 443.2431 [M+Na]$^+$. Its ^{1}H, and ^{13}C NMR spectroscopic data were very similar to those of **38** except that a succinic acid moiety [δ_H 2.56 (2H, m, H-2′), 2.47 (2H, m, H-3′); δ_C 175.0 (s, C-1′), 31.7 (t, C-2′), 32.8 (t, C-3′), 179.4 (s, C-4′)] was located at C-18 in **23**, instead of a carboxyl group in **38**. Therefore, **23** was concluded to be 9,13β-epidioxy-8(14)-abieten-18-succinic acid, and named abiesadine W.

Compound **24** gave the molecular formula $C_{24}H_{38}O_5$, as evidence by its negative HRESIMS at *m/z* 405.2625 [M−H]$^-$. The ^{1}H and ^{13}C NMR spectra were very close to those of **50** except for an additional succinic acid group [δ_H 2.64 (4H, m, H-2′,3′); δ_C 172.5 (s, C-1′), 29.4 (t, C-2′), 29.5 (t, C-3′), 176.7 (s, C-4′)]. By detailed analysis of its 2D NMR spectroscopic data including HSQC, ^{1}H–^{1}H COSY, HMBC, and NOESY, compound **24** was consequently concluded to be torreferol 18-succinic acid, and named abiesadine X.

Compound **25** was assigned the molecular formula $C_{25}H_{40}O_5$, by the positive HRESIMS at *m/z* 443.2743 [M+Na]$^+$. The ^{1}H and ^{13}C NMR spectra were very similar to those of **24** except for an additional methoxy group [δ_H 3.69 (3H, s); δ_C 51.7 (q)]. The C-4′ upfield shift by 4.1 when compared with **24** established the attachment of

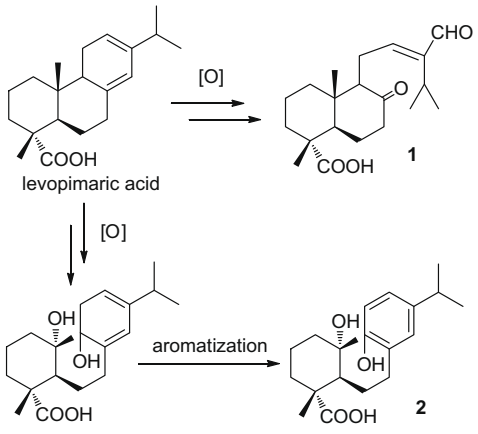

Figure 4. Proposed biosynthetic pathways of abiesadines A and B (**1** and **2**).

Table 3
Anti-inflammatory activities of compounds **1**–**54** isolated from *Abies georgei*

Compounds	IC_{50} (μg/mL)	
	NO[a]	NF-κB[b]
Abiesadine H (**8**)	83.4	>100.0
Abiesadine K (**11**)	52.1	>100.0
Abiesadine P (**16**)	94.1	>100.0
Abiesadine S (**19**)	49.0	>100.0
Abiesadine V (**22**)	56.8	>100.0
Abiesadine Y (**25**)	48.5	22.4
Dehydroabietic acid (**31**)	42.7	>100.0
15-Hydroxydehydroabietic acid (**32**)	76.4	>100.0
13β-Methoxy-7-*oxo*-8(14)-abieten-18-oic acid (**36**)	61.6	>100.0
15-Hydroxy-7-*oxo*-8,11,13-abietatrien-18-oic acid (**47**)	44.0	>100.0
12-Hydroxydehydroabietic acid (**48**)	63.0	>100.0
Manool (**52**)	11.0	>100.0
(8*R*,12*S*,13*S*)-8,12-Epoxy-l3-hydroxylabd-l4-ene (**54**)	21.6	8.7
Others[c]	>100.0	>100.0
Aminoguanidine[d]	3.3	—
Tripterygium glycosides[d]	—	1.0

[a] Effect on NO production induced by LPS in RAW264.7 macrophages.
[b] Effect on NF-κB activities triggered by TNFα in pNF-κB-luc-293 cells.
[c] Other compounds, including **1**–**7**, **9**, **10**, **12**–**15**, **17**, **18**, **20**, **21**, **23**, **24**, **26**–**30**, **33**–**35**, **37**–**46**, **49**, **50**, **51**, and **53**.
[d] Positive control.

the methoxy substituent to the C-4′ carbon of the succinic acid moiety. This was further confirmed by the HMBC correlation of the methoxyl at δ_H 3.69 to C-4′ at δ_C 172.6. Therefore, compound **25** was elucidated as methyl torreferol 18- succinate, and named abiesadine Y.

Abiesadines A and B are two novel *sec*-abietanes. They might have the same precursor, levopimaric acid. The most plausible biosynthesis pathway for these two compounds are the oxidation at C-8 and C-14 of levopimaric acid to form **1**,[5] while the cleavage at C-9 and C-10 of levopimaric acid followed by aromatization to give **2** (Fig. 4).[6,7]

By comparison of the NMR and MS data with the published data, 29 known compounds were identified as pomiferin A (**26**),[8] 18-succinyloxyabieta-8,11,13-triene (**27**),[9] 8,11,13-abietatriene-15,18-diol (**28**),[10] 8,11,13-abietatriene-7α,18-diol (**29**),[11] 7β,18-dihydroxydehydroabietanol (**30**),[12] dehydroabietic acid (**31**), 15-hydroxydehydroabietic acid (**32**),[13] 7-oxodehydroabietinol (**33**),[14] 13β-hydroxy-7-*oxo*-8(14)-abieten-18-oic acid (**34**),[15] 13β,18-dihydroxy-8(14)-abieten-7-one (**35**),[15] 13β-methoxy-7-*oxo*-8(14)-abieten-18-oic acid (**36**),[15] 9,13α-epidioxy-8(14)-abieten-18-oic acid (**37**),[16] 9,13β-epidioxy-8(14)-abieten-18-oic acid (**38**),[16] abieta-7,13-diene-18-oic acid (**39**),[17,18] abietinol-18-succinic acid (**40**),[19] 15-hydroxy-12-*oxo*-7,13-abietadien-18-oic acid (**41**),[13] 7α-hydroxydehydroabietic acid (**42**),[13] 7β-hydroxydehydroabietic acid (**43**),[20] 7β,15-dihydroxydehydroabietic acid (**44**),[21] 7α,15-dihydroxy-8,11,13-abietatrien-18- oic acid (**45**),[22] 7-oxocallitrisic acid (**46**),[23] 15-hydroxy-7-*oxo*-8,11,13-abietatrien-18-oic acid (**47**),[24] 12-hydroxydehydroabietic acid (**48**),[25] 13-*epi*-scloreol (**49**),[26] torreferol (**50**), (8α,12*Z*)-12,14-labdadien-8-ol (**51**),[27] manool (**52**),[28,29] labd-13(*Z*)-ene-8α,15-diol (**53**),[30] and (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**54**).[31]

2.2. Bioactivity assays

In our previous study on the biological activities of *A. georgei* extracts, the $CHCl_3$ fraction showed a strong antiproliferative effect on four tumor cells, especially for LOVO and QGY-7703, while the EtOAc fraction exhibited potent anti-inflammatory effects.[2] Therefore, it was important to investigate the antitumor effects for the isolates from the $CHCl_3$ extract as well as the anti-inflammatory effects for those from the EtOAc extract. In this study, all 54 isolates were tested for bioactivities in order to facilitate elucidating the structure and affect relationships (SARs) of these compounds. In the inhibitory activities against LPS-induced NO production in RAW264.7 macrophages, 13 compounds exhibited moderate effects with IC_{50} value lower than 100 μg/mL. Interestingly, abietanes bearing an 18-succinate are all positive. For those without this moiety, both 18-carbonyl group and a benzoic moiety of the C-ring are necessary. Three labdanes exhibited positive activities, however, they all displayed cytotoxicity (data not shown). In another anti-inflammatory assay against TNFα-triggered NF-κB activity in pNF-κB-luc-293 cells, **25** and **54** demonstrated the strongest activity with IC_{50} values of 22.4 and 8.7 μg/mL, respectively (Table 3).

Table 4
Antiproliferation activities of compounds **1**–**54** isolated from *Abies georgei* against LOVO and QGY-7703 human tumor cell lines (values are IC_{50}, μg/mL)

Compounds	LOVO	QGY-7703
Abiesadine Y (**25**)	10.6	>25.0
Pomiferin A (**26**)	9.2	>25.0
8,11,13-Abietatriene-7α,18-diol (**29**)	9.2	>25.0
7-Oxocallitrisic acid (**46**)	>25.0	10.2
13-*epi*-Scloreol (**49**)	13.0	>25.0
Torreferol (**50**)	24.3	>25.0
(8α,12*Z*)-12,14-Labdadien-8-ol (**51**)	20.3	25.0
(8*R*,12*S*,13*S*)-8,12-Epoxy-l3-hydroxylabd-l4-ene (**54**)	23.1	15.7
Others[a]	>25.0	>25.0
Doxorubicin[b]	0.55	0.42

[a] Other compounds, including **1**–**24**, **27**, **28**, **30**–**45**, **47**, **48**, **52**, and **53**.
[b] Positive control.

For antiproliferation activities of 54 compounds against LOVO tumor cells, seven compounds exhibited potent effects (Table 4). Among them, **26** and **29** exhibited potent effects (IC_{50} = 9.2 μg/mL). In another antiproliferation activities of these compounds against QGY-7703 tumor cells, three compounds (**46**, **51**, and **54**) illustrated the bioactivity with IC_{50} values of 10.2, 25.0, and 15.7 μg/mL, respectively (Table 4).

3. Conclusion

Abies is an important genus of the Pinaceae family. Up to now, ca. 300 chemical constituents were isolated, among which only 26 were diterpenes.[32] Surprisingly, a great number of diterpenes (54 in total) were isolated from *A. georgei*. Therefore, the diterpenoid characteristics are of important chemotaxonomic significance for this plant among *Abies* species in China.

In our previous study, the $CHCl_3$ extract of *A. georgei* showed potent antitumor effects against LOVO and QGY-7703 cells.[2] This was consistent with the results that most of the bioactive antitumor compounds were isolated from $CHCl_3$ fraction.

4. Experimental

4.1. General procedures

1D and 2D NMR spectra were recorded on a Bruker Avance 600 or Avance 300 NMR spectrometer in CD_3OD, $CDCl_3$, or DMSO with TMS as internal standard. ESIMS were measured on a Agilent LC/MSD Trap XCT spectrometer (Waters, USA), and HRESIMS on a Q-TOF micro mass spectrometer (Waters, USA). Optical rotations were acquired with Perkin–Elmer 341 polarimeter. IR spectra were recorded on a Bruker Vector-22 spectrometer with KBr pellets. Materials for CC were silica gel (Huiyou Silical Gel Development Co. Ltd, Yantai, PR China), Sephadex LH-20 (Amersham Pharmacia Biotech AB, Uppsala, Sweden), and YMC-GEL ODS-A (YMC, MA,

USA). Prep. TLC was conducted with glass precoated Silica Gel GF_{254} (Yantai).

4.2. Plant material

The aerial parts of *A. georgei* Orr were collected from Zhongdian city, Yunnan Province of China in July 2006, and were identified by Prof. Li-Shang Xie in Kunming Institute of Botany, Chinese Academy of Sciences. A herbarium specimen (No. 2006-07-016) was deposited in School of Pharmacy, Second Military Medical University, PR China.

4.3. Cell lines used

RAW 264.7, LOVO, and QGY-7703 cells were obtained from Shanghai Institute of Cell Biology, Chinese Academy of Sciences (Shanghai, China), and maintained in media recommended by the suppliers supplemented with 10% fetal bovine serum (FBS) (Gibco, Paisley, UK), and streptomycin (100 mg/mL) in a humidified 5% CO_2 atmosphere at 37 °C.

4.4. Extraction and isolation

The plant material (22 kg) was pulverized and extracted with 80% EtOH under reflux for 3 × 3 h. The extracts were combined to concentrate to a small volume and then partitioned with $CHCl_3$ (25 L), EtOAc (40 L), and *n*-BuOH (50 L), respectively. The EtOAc extract (282 g) was separated into six fractions (F_1–F_6) by CC over silica gel eluting with gradient $CHCl_3$–Me_2CO. Fraction F_1 (36.3 g) was subjected to CC over macroporous resin MCI, Sephadex LH-20, and silica gel to give **27** (149.4 mg, 0.053%*), **37** (51.6 mg, 0.018%*), **38** (34.5 mg, 0.012%*), **39** (20.0 mg, 0.007%*), **40** (29.9 mg, 0.011%*), **51** (18.0 mg, 0.006%*), and **52** (4.2 mg, 0.001%*). Fraction F_2 was divided into 20 subfractions ($F_{2\text{-}1}$–$F_{2\text{-}20}$) by medium pressure liquid chromatography (MPLC) eluting with MeOH–H_2O (5:95–100:0). Compounds **9** (25.8 mg, 0.009%*), **23** (17.6 mg, 0.006%*), and **35** (5.9 mg, 0.002%*) were obtained after CC over LH-20 ($CHCl_3$–MeOH, 1:1) followed by repeated prep. TLC using $CHCl_3$–MeOH (20:1) from subfractions $F_{2\text{-}15}$, $F_{2\text{-}12}$, and $F_{2\text{-}5}$, respectively. From subfraction F_6, **28** (19.3 mg, 0.007%*), **34** (101.9 mg, 0.036%*), and **41** (60.1 mg, 0.021%*) were isolated after CC on LH-20 ($CHCl_3$–MeOH, 1:1) and prep. TLC using $CHCl_3$–MeOH (20:1) or petroleum ether–EtOAc (1:1). By the same ways, **17** (29.2 mg, 0.010%*), **30** (36.7 mg, 0.013%*), and **31** (200.2 mg, 0.071%*) were obtained from subfraction $F_{2\text{-}7}$, **33** (16.0 mg, 0.006%*) and **36** (125.7 mg, 0.045%*) from subfraction $F_{2\text{-}9}$; **1** (2.5 mg, 0.001%*), **5** (9.4 mg, 0.003%*), **16** (6.6 mg, 0.002%*), **32** (26.3 mg, 0.009%*), **46** (103.5 mg, 0.037%*), and **53** (15.9 mg, 0.006%*) from subfraction $F_{2\text{-}11}$, and **6** (25.0 mg, 0.009%*), **29** (56.7 mg, 0.020%*), **42** (25.0 mg, 0.009%*) from subfraction $F_{2\text{-}18}$, respectively. Fraction F_3 was subjected to CC over ODS [MeOH–H_2O (5:95–100:0)] and LH-20 ($CHCl_3$–MeOH, 1:1; MeOH), followed by prep. TLC using $CHCl_3$–MeOH (20:1) and/or petroleum ether–EtOAc (1:1) led to the isolation of **7** (8.7 mg, 0.003%*), **10** (6.4 mg, 0.002%*), **14** (32.1 mg, 0.011%*), **20** (7.1 mg, 0.003%*), **21** (16.4 mg, 0.006%*), and **47** (143.3 mg, 0.051%*). Similarly, **4** (3.7 mg, 0.001%*), **13** (7.0 mg, 0.003%*), **15** (21.0 mg, 0.007%*), **18** (5.7 mg, 0.002%*), and **44** (58.7 mg, 0.021%*) were isolated from fraction F_4; while **12** (7.9 mg, 0.003%*) and **45** (18.7 mg, 0.007%*) from fraction F_6. The $CHCl_3$ extract (906 g) was separated into five fractions (F_{C1}–F_{C5}) by CC over silica gel eluting with gradient petroleum ether–$CHCl_3$. Compounds **2** (5.6 mg, 0.006‰**), **26** (4.2 mg, 0.005‰**), **50** (46.2 mg, 0.051‰**), and **54** (6.0 mg, 0.007‰**) were purified from fraction F_{C2} after repeated CC over LH-20 eluting with $CHCl_3$–MeOH (1:1) and MeOH, followed by prep. TLC using $CHCl_3$–MeOH (100:1) and/or petroleum ether–EtOAc (4:1). By the similar procedures, **48** (17.4 mg, 0.019‰**) and **49** (25.8 mg, 0.028‰**) were isolated from fraction F_{C3}, and **3** (7.0 mg, 0.008‰**), **8** (33.3 mg, 0.037‰**), **9** (77.6 mg, 0.086‰**), **11** (12.6 mg, 0.014‰**), **19** (24.6 mg, 0.027‰**), **22** (5.1 mg, 0.006‰**), **24** (368.2 mg, 0.406‰**), **25** (39.4 mg, 0.043‰**), and **43** (4.5 mg, 0.005‰**) from fraction F_{C4}. (Percentage yields calculated as weight to weight estimates in *282 g of EtOAc extract and **906 g of $CHCl_3$ extract.)

Abiesadine A (**1**)*:* Amorphous powder; $[\alpha]_D^{25}$ −14.0 (*c* 0.05, MeOH); IR (KBr) ν_{max} 3447, 2970, 2945, 1738, 1684, 1383, 1229, 1216, 899 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 357 $[M+Na]^+$; ESIMS (negative) *m/z* 333 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 357.2046, calcd for $C_{20}H_{30}O_4Na$, 357.2042.

Abiesadine B (**2**)*:* Amorphous powder; $[\alpha]_D^{20}$ +8.0 (*c* 0.30, MeOH); IR (KBr) ν_{max} 3421, 2932, 2869, 1698, 1653, 1559, 1497, 1458, 1384, 1246, 1175, 1097, 1034, 906, 822, 668 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 357 $[M+Na]^+$; ESIMS (negative) *m/z* 333 $[M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 333.2096, calcd for $C_{20}H_{29}O_4$, 333.2066.

Abiesadine C (**3**)*:* Amorphous powder; $[\alpha]_D^{20}$ +23.3 (*c* 0.24, MeOH); IR (KBr) ν_{max} 3485, 2964, 2922, 1703, 1470, 1386, 1258, 1172, 1047, 1022, 991, 930, 902, 826, 654 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 375 $[M+Na]^+$, 727 $[2M+Na]^+$; ESIMS (negative) *m/z* 351 $[M-H]^-$, 703 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 351.2176, calcd for $C_{20}H_{31}O_5$, 351.2171.

Abiesadine D (**4**)*:* Amorphous powder; $[\alpha]_D^{20}$ +7.4 (*c* 0.30, MeOH); IR (KBr) ν_{max} 3443, 2927, 1737, 1653, 1384, 1229, 1217, 1047 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 375 $[M+Na]^+$, 727 $[2M+Na]^+$; ESIMS (negative) *m/z* 351 $[M-H]^-$, 387 $[M+Cl]^-$, 703 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 351.2172, calcd for $C_{20}H_{32}O_5$, 351.2171.

Abiesadine E (**5**)*:* Amorphous powder; $[\alpha]_D^{20}$ −29.9 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3433, 2961, 2927, 2830, 1726, 1672, 1629, 1596, 1363, 1243, 1043, 774 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 339 $[M+Na]^+$, 655 $[2M+Na]^+$; ESIMS (negative) *m/z* 315 $[M-H]^-$, 631 $[2M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 339.1950, calcd for $C_{20}H_{28}O_3Na$, 339.1936.

Abiesadine F (**6**)*:* Amorphous powder; $[\alpha]_D^{20}$ −1.3 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3396, 2962, 2926, 2866, 1737, 1724, 1565, 1497, 1396, 1252, 1172, 1025, 956, 825 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 425 $[M+Na]^+$; ESIMS (negative) *m/z* 401 $[M-H]^-$, 437 $[M+Cl]^-$. HRESIMS (positive) $[M+Na]^+$ *m/z* 425.2293, calcd for $C_{24}H_{34}O_5Na$, 425.2304.

Abiesadine G (**7**)*:* Amorphous powder; $[\alpha]_D^{20}$ +8.9 (*c* 0.52, MeOH); IR (KBr) ν_{max} 3440, 2958, 2931, 2869, 2822, 1735, 1685, 1585, 1459, 1384, 1254, 1168, 1079, 999, 768 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 439 $[M+Na]^+$; ESIMS (negative) *m/z* 415 $[M-H]^-$, 831 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 415.2571, calcd for $C_{25}H_{35}O_5$, 415.2484.

Abiesadine H (**8**)*:* Amorphous powder; $[\alpha]_D^{20}$ +3.0 (*c* 0.41, MeOH); IR (KBr) ν_{max} 2960, 2927, 2853, 1739, 1498, 1382, 1159, 1029, 999, 827 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 439 $[M+Na]^+$, 855 $[2M+Na]^+$; ESIMS (negative) *m/z* 451 $[M+Cl]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 439.2490, calcd for $C_{25}H_{36}O_5Na$, 439.2460.

Abiesadine I (**9**)*:* Amorphous powder; $[\alpha]_D^{20}$ +13.5 (*c* 0.35, MeOH); IR (KBr) ν_{max} 3444, 2965, 2928, 2850, 1740, 1713, 1559, 1499, 1471, 1379, 1260, 1219, 1162, 1002 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 425 $[M+Na]^+$, 827 $[2M+Na]^+$; ESIMS (negative) *m/z* 401 $[M-H]^-$, 437 $[M+Cl]^-$, 803 $[2M-H]^-$, 840 $[2M+Cl]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 425.2312, calcd for $C_{24}H_{34}O_6Na$, 425.2304.

Abiesadine J (**10**)*:* Amorphous powder; $[\alpha]_D^{20}$ +10.5 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3442,2979, 2928, 2852, 1744, 1709, 1607, 1497, 1381, 1261, 1169 1075, 998, 827 cm^{-1}; for ^1H and ^{13}C

NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 439 $[M+Na]^+$; ESIMS (negative) *m/z* 415 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 439.2459, calcd for $C_{25}H_{36}O_5Na$, 439.2460.

Abiesadine K (**11**)*:* Amorphous powder; $[\alpha]_D^{20}$ +22.8 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3447, 2970, 2930, 2869, 1738, 1653, 1456, 1366, 1228, 1160, 1001, 896 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 439 $[M+Na]^+$, 853 $[2M+Na]^+$; ESIMS (negative) *m/z* 415 $[M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 415.2473, calcd for $C_{25}H_{35}O_5$, 415.2484.

Abiesadine L (**12**)*:* Amorphous powder; $[\alpha]_D^{20}$ +2.0 (*c* 0.24, MeOH); IR (KBr) ν_{max} 3431, 2967, 2931, 2869, 1734, 1458, 1384, 1255, 1166, 1046, 859 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 441 $[M+Na]^+$; ESIMS (negative) *m/z* 417 $[M-H]^-$, 453 $[M+Cl]^-$, 835 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 417.2278, calcd for $C_{24}H_{33}O_6$, 417.2277.

Abiesadine M (**13**)*:* Amorphous powder; $[\alpha]_D^{20}$ +4.0 (*c* 0.43, MeOH); IR (KBr) ν_{max} 3440, 2932, 2869, 1735, 1497, 1384, 1257, 1169, 1073, 832 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 455 $[M+Na]^+$, 887 $[2M+Na]^+$; ESIMS (negative) *m/z* 431 $[M-H]^-$, 467 $[M+Cl]^-$, 863 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 431.2435, calcd for $C_{25}H_{35}O_6$, 431.2434.

Abiesadine N (**14**)*:* Amorphous powder; $[\alpha]_D^{20}$ +16.5 (*c* 0.35, MeOH); IR (KBr) ν_{max} 3432, 2976, 2931, 2868, 1697, 1561, 1460, 1384, 1258, 1173, 1075, 828 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 353 $[M+Na]^+$, 683 $[2M+Na]^+$; ESIMS (negative) *m/z* 329 $[M-H]^-$, 659 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 329.2116, calcd for $C_{21}H_{29}O_3$, 329.2117.

Abiesadine O (**15**)*:* Amorphous powder; $[\alpha]_D^{20}$ +2.0 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3290, 2976, 2928, 2453, 2059, 1715, 1497, 1441, 1364,1296, 1222, 1051, 851, 642 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 369 $[M+Na]^+$, 715 $[2M+Na]^+$; ESIMS (negative) *m/z* 691 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 345.2064, calcd for $C_{21}H_{29}O_4$, 345.2066.

Abiesadine P (**16**)*:* Amorphous powder; $[\alpha]_D^{20}$ +0.3 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3432, 2976, 2928, 2831, 1630, 1605, 1467, 1364, 1254, 1165, 1106, 1070, 775 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 367 $[M+Na]^+$; ESIMS (negative) *m/z* 343 $[M-H]^-$. HRESIMS (positive) $[M+Na]^+$ *m/z* 367.2304, calcd for $C_{22}H_{32}O_3Na$, 367.2249.

Abiesadine Q (**17**)*:* Amorphous powder; $[\alpha]_D^{20}$ +0.3 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3447, 2958, 2931, 2870, 1736, 1682, 1383, 1300, 1162, 1058, 835 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 423 $[M+Na]^+$, 823 $[2M+Na]^+$; ESIMS (negative) *m/z* 399 $[M-H]^-$, 435 $[M+Cl]^-$, 799 $[2M-H]^-$. HRESIMS (negative) $[M-H]^-$ *m/z* 399.2128, calcd for $C_{24}H_{31}O_5$, 399.2171.

Abiesadine R (**18**)*:* Amorphous powder; $[\alpha]_D^{20}$ +3.0 (*c* 0.5, MeOH); IR (KBr) ν_{max} 3439, 2972, 2930, 2853, 1739, 1679, 1606, 1469, 1383, 1258, 1161, 999, 839, 617 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 439 $[M+Na]^+$; ESIMS (negative) *m/z* 415 $[M-H]^-$, 451 $[M+Cl]^-$, 831 $[2M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 439.2107, calcd for $C_{24}H_{32}O_6Na$, 439.2097; HRESIMS (negative) $[M-H]^-$ *m/z* 415.2133, calcd for $C_{24}H_{31}O_6$, 415.2121.

Abiesadine S (**19**)*:* Amorphous powder; $[\alpha]_D^{20}$ −3.3 (*c* 0.45, MeOH); IR (KBr) ν_{max} 3461, 2972, 2927, 2852, 1742, 1679, 1607, 1492, 1466, 1440, 1411, 1364, 1258, 1158, 1028, 999, 842, 618 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 453 $[M+Na]^+$, 883 $[2M+Na]^+$; ESIMS (negative) *m/z* 429 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 453.2286, calcd for $C_{25}H_{34}O_6Na$, 453.2253.

Abiesadine T (**20**)*:* Amorphous powder; $[\alpha]_D^{20}$ −14.0 (*c* 0.21, MeOH); IR (KBr) ν_{max} 3446, 2942, 2873, 2826, 1596, 1394, 1355, 1079, 1006 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 471 $[M+Na]^+$, 719 $[2M+Na]^+$; ESIMS (negative) *m/z* 347 $[M-H]^-$, 939 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 347.2220, calcd for $C_{21}H_{31}O_4$, 347.2222.

Abiesadine U (**21**)*:* Amorphous powder; $[\alpha]_D^{20}$ −0.1 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3465, 2963, 2928, 2851, 1741, 1711, 1681, 1608, 1467, 1384, 1259, 1159, 1067, 997, 833 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 457 $[M+Na]^+$, 891 $[2M+Na]^+$; ESIMS (negative) *m/z* 469 $[M+Cl]^-$, 867 $[2M-H]^-$. HRESIMS (positive) $[M+Na]^+$ *m/z* 457.2509, calcd for $C_{25}H_{38}O_6Na$, 457.2566.

Abiesadine V (**22**)*:* Amorphous powder; $[\alpha]_D^{20}$ +20.8 (*c* 0.30, MeOH); IR (KBr) ν_{max} 2958, 2927, 2851, 1738, 1651, 1617, 1559, 1472, 1368, 1263, 1158, 994 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 435 $[M+H]^+$, 457 $[M+Na]^+$, 891 $[2M+Na]^+$; ESIMS (negative) *m/z* 433 $[M-H]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 457.2565, calcd for $C_{25}H_{38}O_6Na$, 457.2566.

Abiesadine W (**23**)*:* Amorphous powder; $[\alpha]_D^{20}$ −0.4 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3433, 2964, 2928, 2779, 1727, 1614, 1586, 1408, 1372, 1258, 1162, 773 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 443 $[M+Na]^+$; ESIMS (negative) *m/z* 419 $[M-H]^-$, 455 $[M+Cl]^-$. HRESIMS (positive) $[M+Na]^+$ *m/z* 443.2431, calcd for $C_{24}H_{36}O_6Na$, 443.2410.

Abiesadine X (**24**)*:* Amorphous powder; $[\alpha]_D^{20}$ +31.8 (*c* 1.15, MeOH); IR (KBr) ν_{max} 3445, 2932, 2853, 1736, 1643, 1442, 1383, 1218, 1166, 996, 919, 892, 828 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 429 $[M+Na]^+$; ESIMS (negative) *m/z* 405 $[M-H]^-$, 441 $[M+Cl]^-$, 811 $[2M-H]^-$; HRESIMS (negative) $[M-H]^-$ *m/z* 405.2625, calcd for $C_{24}H_{37}O_5$, 405.2641.

Abiesadine Y (**25**)*:* Amorphous powder; $[\alpha]_D^{20}$ +17.0 (*c* 0.50, MeOH); IR (KBr) ν_{max} 3445, 2969, 2928, 2851, 1741, 1642, 1466, 1440, 1319, 1161, 998, 919, 847 cm^{-1}; for ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive) *m/z* 443 $[M+Na]^+$, 863 $[2M+Na]^+$; ESIMS (negative) *m/z* 465 $[M+Cl]^-$; HRESIMS (positive) $[M+Na]^+$ *m/z* 443.2743, calcd for $C_{25}H_{40}O_5Na$, 443.2773.

8,11,13-Abietatriene-15,18-diol (**28**)*:* Amorphous powder; ^1H NMR data (CD_3OD, 300 MHz): δ 7.17 (2H, m, H-11,12), 7.10 (1H, br s, H-14),3.44 (1H, d, J = 10.2 Hz, H-18a), 3.09 (1H, d, J = 10.2 Hz, H-18b), 1.48 (6H, s, Me-16,17), 1.19 (3H, s, Me-20), 0.86 (3H, s Me-19); ^{13}C NMR data, see Table 2; ESIMS (positive) *m/z* 325 $[M+Na]^+$, 627 $[2M+Na]^+$.

8,11,13-Abietatriene-7α,18-diol (**29**)*:* Amorphous powder; ^1H NMR data (CD_3OD, 300 MHz): δ 7.19 (1H, d, J = 8.4 Hz, H-11), 7.17 (1H, d, J = 2.1 Hz, H-14), 7.08 (1H, dd, J = 8.4, 2.1 Hz, H-12), 4.72 (1H, dd, J = 3.3, 1.5 Hz, H-7), 3.40 (1H, d, J = 11.1 Hz, H-18a), 3.20 (1H, d, J = 11.1 Hz, H-18b), 2.84 (1H, sep, J = 6.9 Hz, H-15), 1.22 (6H, d, J = 6.9 Hz, Me-16,17), 1.14 (3H, s, Me-20), 0.89 (3H, s, Me-19); ^{13}C NMR data, see Table 2; ESIMS (positive) *m/z* 325 $[M+Na]^+$, 627 $[2M+Na]^+$; ESIMS (negative) *m/z* 337 $[M+Cl]^-$.

15-Hydroxydehydroabietic acid (**32**)*:* Amorphous powder; ^1H NMR data (CD_3OD, 300 MHz): δ 7.17 (1H, br s, H-11), 7.17 (1H, br s, H-12), 7.09 (1H, s, H-14), 1.47 (6H, s, Me-16,17), 1.22 (3H, s, Me-20), 1.18 (3H, s Me-19); ^{13}C NMR data, see Table 2; ESIMS (positive) *m/z* 339 $[M+Na]^+$, 655 $[2M+Na]^+$; ESIMS (negative) *m/z* 315 $[M-H]^-$, 631 $[2M-H]^-$.

13β,18-Dihydroxy-8(14)-abieten-7-one (**35**)*:* Amorphous powder; ^1H NMR data (CD_3OD, 300 MHz): δ 6.68 (1H, dd, J = 2.7, 1.8 Hz, H-14), 3.29 (1H, m, H-18a), 2.97 (1H, d, J = 11.4 Hz, H-18b), 2.52 (1H, dd, J = 18.6, 5.1 Hz, H-6a), 2.30 (1H, dd, J = 18.6, 13.5 Hz, H-6b), 0.94 (3H, d, J = 6.9 Hz, Me-17), 0.90 (3H, s, Me-20), 0.84 (3H, s Me-19), 0.83 (3H, d, J = 6.9 Hz, Me-17); ^{13}C NMR data, see Table 2; ESIMS (positive) *m/z* 343 $[M+Na]^+$, 663 $[2M+Na]^+$; ESIMS (negative) *m/z* 319 $[M-H]^-$, 355 $[M+Cl]^-$, 639 $[2M-H]^-$.

13β-Methoxy-7-oxo-8(14)-abieten-18-oic acid (**36**)*:* Amorphous powder; ^1H NMR data (CD_3OD, 300 MHz): δ 6.69 (1H, br s, H-14), 1.20 (3H, s, Me-19), 0.89 (3H, s, Me-20), 0.88 (3H, d, J = 6.9 Hz, Me-16), 0.78 (3H, d, J = 7.1 Hz, Me-17); ^{13}C NMR data, see Table 2; ESIMS (positive) *m/z* 371 $[M+Na]^+$; ESIMS (negative) *m/z* 347 $[M-H]^-$.

9,13β-Epidioxy-8(14)-abieten-18-oic acid (**38**)*:* Amorphous powder; ^{1}H NMR data (CD_3OD, 300 MHz): δ 6.15 (1H, t, J = 2.2 Hz, H-14), 1.27 (3H, s, Me-19), 1.08 (3H, s, Me-20), 0.96 (3H, d, J = 6.8 Hz, Me-16), 0.95 (3H, d, J = 6.8 Hz, Me-17); ^{13}C NMR data, see Table 2; ESIMS (positive) m/z 357 $[M+Na]^+$, 691 $[2M+Na]^+$; ESIMS (negative) m/z 333 $[M-H]^-$.

13-epi-Sclareol (**49**)*:* Amorphous powder; ^{1}H NMR data (CD_3OD, 300 MHz): δ 5.88 (1H, dd, J = 17.4, 10.8 Hz, H-14), 5.18 (1H, dd, J = 17.4, 1.6 Hz, H-15a), 5.01 (1H, dd, J = 10.8, 1.6 Hz, H-15b), 1.22 (3H, s, Me-16), 1.10 (3H, s, Me-17), 0.87 (3H, s, Me-18), 0.80 (3H, s, Me-20); ^{13}C NMR data, see Table 2; ESIMS (positive) m/z 331 $[M+Na]^+$, 639 $[2M+Na]^+$; ESIMS (negative) m/z 344 $[M+Cl]^-$.

4.5. Assays for anti-inflammatory and antitumor activities

These two experiments were carried out according to the previously reported procedures.[2]

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmc.2009.11.055.

References and notes

1. Zheng, W. J.; Fu, L. G.. In *Flora of China*; Wu, Z. Y., Ed.; Science Press: Beijing, 1978; Vol. 7, pp 77–78.
2. Yang, X. W.; Zeng, H. W.; Liu, X. H.; Li, S. M.; Xu, W.; Shen, Y. H.; Zhang, C.; Zhang, W. D. *J. Pharm. Pharmacol.* **2008**, *60*, 937.
3. Yang, X. W.; Li, S. M.; Feng, L.; Shen, Y. H.; Tian, J. M.; Liu, X. H.; Zeng, H. W.; Zhang, C.; Zhang, W. D. *Tetrahedron* **2008**, *64*, 4354.
4. Yang, X. W.; Li, S. M.; Feng, L.; Shen, Y. H.; Tian, J. M.; Zeng, H. W.; Liu, X. H.; Shan, L.; Su, J.; Zhang, C.; Zhang, W. D. *Tetrahedron Lett.* **2008**, *49*, 3042.
5. Lee, C. K.; Cheng, Y. S. *J. Nat. Prod.* **2001**, *64*, 511.
6. Pellegata, R.; Dosi, I.; Villa, M.; Lesma, G.; Palmisano, G. *Tetrahedron* **1985**, *41*, 5607.
7. Yin, C. X.; Xiao, H.; Gao, Z. L.; Huang, R.; Zhang, S.; Liu, F. C. *J. Yunnan Univ.* **2005**, *27*, 437.
8. Fraga, B. M.; Mestres, T.; Diaz, C. E.; Arteaga, J. M. *Phytochemistry* **1994**, *35*, 1509.
9. Raldugin, V. A.; Grishko, V. V.; Kukina, T. P.; Druganov, A. G.; Shakirov, M. M. *Russ. Chem. Bull.* **2005**, *54*, 1747.
10. Conner, A. H.; Rowe, J. W. *Phytochemistry* **1977**, *16*, 1777.
11. Barrero, A. F.; Sanchez, J. F.; Alvarez-Manzaneda, E. J.; Munoz, M.; Haidour, A. *Phytochemistry* **1992**, *31*, 615.
12. Ohmoto, T.; Saito, M.; Yamaguchi, K. *Chem. Pharm. Bull.* **1987**, *35*, 2443.
13. Cheung, H. T. A.; Miyase, T.; Lenguyen, M. P.; Smal, M. A. *Tetrahedron* **1993**, *49*, 7903.
14. Tanaka, R.; Ohtsu, H.; Matsunaga, S. *Phytochemistry* **1997**, *44*, 1051.
15. Ohtsu, H.; Tanaka, R.; In, Y.; Matsunaga, S.; Tokuda, H.; Nishino, H. *Can. J. Chem.* **2000**, *78*, 31.
16. Barrero, A. F.; Sanchez, J. F.; Alvarez-Manzaneda, E. J.; Dorado, M. M.; Haidour, A. *Phytochemistry* **1991**, *30*, 593.
17. Smite, E.; Lundgren, L.; Andersson, R. *Phytochemistry* **1993**, *32*, 365.
18. Zdero, C.; Bohlmann, F.; Niemeyer, H. M. *Phytochemistry* **1991**, *30*, 3669.
19. Raldugin, V. A.; Demenkova, L. I.; Pentegova, V. A. *Chem. Nat. Compd.* **1990**, *26*, 594.
20. Gouiric, S. C.; Feresin, G. E.; Tapia, A. A.; Rossomando, P. C.; Schmeda-Hirschmann, G.; Bustos, D. A. *World J. Microb. Biot.* **2004**, *20*, 281.
21. Ohmoto, T.; Kanatani, K.; Yamaguchi, K. *Chem. Pharm. Bull.* **1987**, *35*, 229.
22. Prinz, S.; Mullner, U.; Heilmann, J.; Winkelmann, K.; Sticher, O.; Haslinger, E.; Hufner, A. *J. Nat. Prod.* **2002**, *65*, 1530.
23. Kim, Y. G.; Lee, H.; Ozawa, S.; Sasaya, T.; Moon, C. K. *Mokuzai Gakkaishi* **1994**, *40*, 414.
24. Matsumoto, T.; Imai, S.; Sunaoka, Y.; Yoshinari, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 723.
25. Kinouchi, Y.; Ohtsu, H.; Tokuda, H.; Nishino, H.; Matsunaga, S.; Tanaka, R. *J. Nat. Prod.* **2000**, *63*, 817.
26. Torrenegra, R.; Pedrozo, J.; Robles, J.; Waibel, R.; Achenbach, H. *Phytochemistry* **1992**, *31*, 2415.
27. Barrero, A. F.; Altarejos, J. *Magn. Reson. Chem.* **1993**, *31*, 299.
28. Ulubelen, A.; Topcu, G.; Eris, C.; Sonmez, U.; Kartal, M.; Kurucu, S.; Bozok-Johansson, C. *Phytochemistry* **1994**, *36*, 971.
29. Conner, A. H.; Rowe, J. W. *Phytochemistry* **1976**, *15*, 1949.
30. Schmidt, T. J.; Passreiter, C. M.; Wendisch, D.; Willuhn, G. *Phytochemistry* **1995**, *40*, 1213.
31. Wahlberg, I.; Karlsson, K.; Nishida, T.; Cheng, K. P.; Enzell, C. R.; Berg, J. E.; Pilotti, A. M. *Acta Chem. Scand.* **1977**, *31B*, 453–459.
32. Yang, X. W.; Li, S. M.; Shen, Y. H.; Zhang, W. D. *Chem. Biodivers.* **2008**, *5*, 56.