Terpenoid Constituents of *Abies chensiensis* with Potential Anti-inflammatory Activity

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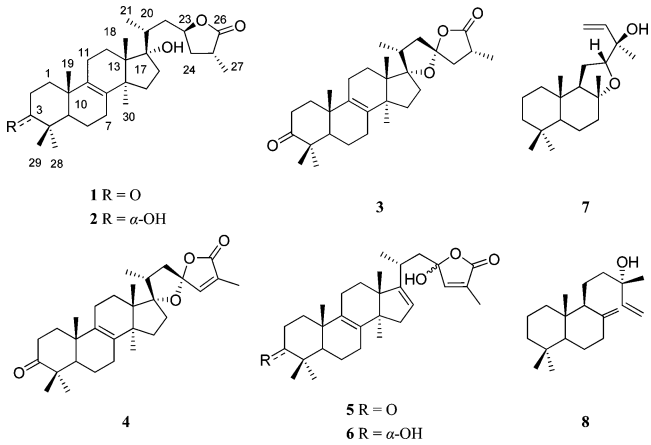
Six new triterpenes (neoabieslactones A−F, **1**−**6**) and 17 known compounds were isolated from the aerial parts of *Abies chensiensis.* The structures of the new triterpenes were proposed by 1D and 2D NMR spectroscopy. Compound **1** was confirmed structurally by X-ray crystallography. In a bioassay against LPS-induced NO production in RAW264.7 macrophages, three compounds, neoabieslactone E (**5**), (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**7**), and manool (**8**), exhibited IC_{50} values of 9.1, 1.9, and 9.6 μg/mL, respectively.

Abies is an important genus of the Pinaceae family. Previous phytochemical investigations on this species have afforded ca. 300 compounds including terpenoids, flavonoids, lignans, and miscellaneous constituents.[1−5] Crude extracts and metabolites of *Abies* plants are reported to have a broad range of bioactivities, such as anti-inflammatory, antihypertensive, and cytotoxic effects.[2] Previously, investigations on *A. georgei* have been carried out in our laboratory.[6−8] In our continuing investigations on *Abies* species occurring in mainland China, *A. chensiensis* was selected for study.

Abies chensiensis Van Tiegh is a woody plant distributed mainly in Shaanxi and Hubei Provinces of the People's Republic of China.[9] Previously, 23 phenolics with chemotaxonomic significance were isolated from this plant.[10] Herein, we report the isolation and structural elucidation of six new triterpenes (**1**−**6**). Also obtained were 17 known triterpenoids, diterpenoids, norditerpenoids, and monoterpenoids. In addition, the potential anti-inflammatory activity of all isolates obtained against lipopolysaccharide (LPS)-induced NO production in macrophages is described in this paper.



Results and Discussion

Compound **1** gave the molecular formula $C_{30}H_{46}O_4$ in the negative HRESIMS at *m*/*z* 469.3315 $[M - H]^-$, indicating eight degrees of unsaturation. The ^1H, ^{13}C, and DEPT NMR spectra of

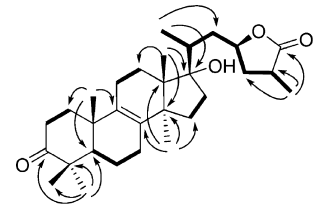


Figure 1. Selected $^1H-^1H$ COSY (bold) and HMBC (arrow) correlations of **1**.

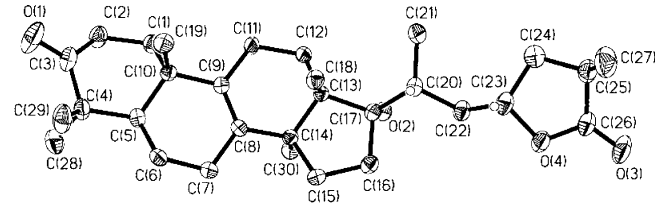


Figure 2. X-ray crystal structure diagram of **1**.

1 showed the presence of five singlet and two doublet methyls [δ_H 0.86 (3H, s, Me-18), 1.13 (3H, s, Me-19), 0.99 (3H, d, $J = 6.6$ Hz, Me-21), 1.30 (3H, d, $J = 7.8$ Hz, Me-27), 1.10 (3H, s, Me-28), 1.08 (3H, s, Me-29), 1.16 (3H, s, Me-30); δ_C 18.6 (C-18), 18.5 (C-19), 14.2 (C-21), 15.9 (C-27), 26.2 (C-28), 21.3 (C-29), 26.3 (C-30)], 10 methylenes, four methines, and nine quaternary carbons including two olefinic carbons [δ_C 136.4 (C-8), 132.7 (C-9)], one oxygen-bearing quaternary carbon [δ_C 85.5 (C-17)], and two carbonyls [δ_C 217.6 (C-3), 180.2 (C-26)]. Analysis of the $^1H-^1H$ COSY spectrum of **1** showed five $^1H-^1H$ spin systems, from which five fragments were assigned as H_2-1/H_2-2, H-5/H_2-6/H_2-7, H_2-11/H_2-12, H_2-15/H_2-16, and H_3-21/H-20/H_2-22/H-23/H_2-24/H-25/H_3-27 (Figure 1). In the HMBC spectrum, correlations from seven methyls were used to establish the planar structure of **1** as 17-hydroxy-3-oxolanosta-8-en-26,23-olide (Figure 1). The relative configuration of **1** was established unambiguously by single-crystal X-ray diffraction (Figure 2), which was consistent with those correlations in its NOESY spectrum (Supporting Information, Figure S6). In the circular dichroism (CD) spectrum, a negative Cotton effect at 223 nm (−9.4) was found, which established a 23*R* configuration of the lactone side chain in **1**.[11,12] Accordingly, the structure of compound **1** was proposed as (5*R*,17*S*,23*R*,25*R*)-17-hydroxy-3-oxolanosta-8-en-26,23-olide, and this compound has been named neoabieslactone A.

Compound **2** was found to possess the molecular formula $C_{30}H_{48}O_4$ from the positive HRESIMS at *m*/*z* 495.3463 $[M + Na]^+$,

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Table 1. ^{1}H NMR Spectroscopic Data of Compounds **1**−**6** in $CDCl_3$ (*J* values in Hz)

position	**1**[a]	**2**[a]	**3**[b]	**4**[b]	**5**[c]	**6**[d]
1	1.62 m; 1.99 m	1.44 m; 1.55 m	1.61 m; 1.93 m	1.60 m; 1.96 m	1.61 m; 1.97 m	1.50 m; 1.58 m
2	2.42 m; 2.58 m	1.58 m; 1.92 m	2.40 m; 2.60 m	2.40 m; 2.60 m	2.40 m; 2.58 m	1.60 m; 1.95 m
3		3.40 br s				3.44 br s
5	1.60 m	1.48 m	1.62 m	1.61 m	1.62 m	1.52 m
6	2.08 m	2.02 m	2.08 m	2.09 m	2.16 m	2.10 m
7	2.12 m	2.08 m	2.08 m	2.08 m	2.10 m	2.08 m
11	1.62 m	1.60 m	1.62 m	1.61 m	1.64 m	1.62 m
12	1.52 m; 2.11 m	1.44 m; 2.05 m	1.44 m; 2.12 m	1.48 m; 2.09 m	1.52 m	1.51 m
15	1.41 m; 1.69 m	1.19 m; 1.80 m	1.37 m; 1.77 m	1.41 m; 1.71 m	1.76 m; 2.40 m	1.78 m, 2.43 m
16	1.88 m; 1.98 m	1.51 m; 2.40 m	1.77 m; 2.03 m	1.87 m; 2.02 m	5.34 br s	5.41 br s
18	0.86 s	0.89 s	0.94 s	0.96 s	0.77 s	0.84 s
19	1.13 s	0.96 s	1.12 s	1.10 s	1.12 s	1.00 s
20	2.06 m	2.18 m	2.27 m	2.37 m	2.03 m	2.03 m
21	0.99 (d, 6.6)	1.06 (d, 6.6)	1.06 (d, 7.2)	1.11 (d, 7.0)	1.07 (d, 6.6)	1.08 (d, 6.8)
22	1.80 m; 2.00 m	1.31 m; 1.98 m	1.77 m; 2.73 m	1.84 m; 2.67 m	1.97 m; 2.29 m	1.85 m; 2.30 m
23	4.60 br s	4.60 br s				
24	2.04 m; 2.09 m	2.05 m	2.02 m; 2.48 m	6.69 s	6.76 s	6.80 s
25	2.72 m	2.68 m	2.97 m			
27	1.30 (d, 7.8)	1.26 (d, 7.2)	1.26 (d, 7.2)	1.90 s	1.90 s	1.90 s
28	1.10 s	0.95 s	1.10 s	1.09 s	1.10 s	0.98 s
29	1.08 s	0.85 s	1.07 s	1.06 s	1.06 s	0.88 s
30	1.16 s	0.94 s	1.04 s	1.07 s	0.96 s	0.95 s

[a] Recorded at 600 MHz. [b] Recorded at 300 MHz. [c] Recorded at 500 MHz. [d] Recorded at 400 MHz.

indicating seven degrees of unsatutation. The ^{1}H and ^{13}C NMR spectra of **2** were almost the same as those of **1**. However, comparison of the ^{13}C NMR spectrum of these two compounds showed a major difference: a ketone group at δ_C 217.6 was absent, while an oxygenated methine signal appeared at δ_C 75.8 in **2**. This implied that a hydroxy group is located at C-3 in **2** instead of the carbonyl group in **1**. The assumption was confirmed by the correlations of Me-28 and 29 to C-3 (δ_C 75.8) in the HMBC experiment. According to the NOESY correlations of H_3-19 to H_3-29 and H_3-29 to H-3, compound **2** (neoabieslactone B) was thus proposed as (3*R*,5*R*,17*S*,23*R*,25*R*)-3,17-dihydroxylanosta-8-en-26,23-olide.

Compound **3** was assigned the molecular formula $C_{30}H_{44}O_4$ from the positive HRESIMS at *m*/*z* 491.3154 $[M + Na]^+$, indicating nine degrees of unsaturation. Close comparison of the ^{13}C NMR spectrum of compound **3** to that of **1** showed a general similarity, except for the presence of a hemiacetal quaternary carbon at δ_C 113.5 at the C-23 position of **3** instead of the oxygenated methine signal at δ_C 77.1 of **1**. Taking the molecular formula into consideration, **3** was deduced as having a spiro structure. The configuration at C-17 of compound **3** was assigned as *S* since the C-12 signal resonated at a higher field (5.0 ppm) as compared with that of neoabieslactone, owing to the upfield shift caused by the C-17α oxygen atom.[13,14] Such an effect was also found for compounds **1** and **2**. In addition, according to the negative Cotton effect at 218 nm ($\Delta\varepsilon = -8.0$) of **3**, C-23 of the lactone side chain was assigned as having an *R* configuration. Therefore, compound **3** (neoabieslactone C) was deduced as (5*R*,17*S*,23*R*,25*R*)-17,23-epoxy-3-oxolanosta-8-en-26,23-olide.

Compound **4** gave a molecular formula of $C_{30}H_{42}O_4$, as determined from the negative HRESIMS at *m*/*z* 465.2988 $[M - H]^-$. The IR spectrum showed the presence of a saturated carbonyl group (1708 cm^{-1}) and an α,β-unsaturated butyrolactone (1759 cm^{-1}). Comparison with **3** showed almost the same physical and NMR spectroscopic data for **4**, except for the olefinic bond located at the C-24,25 positions (δ_C 147.2, 130.4). By detailed analysis of its HSQC, ^{1}H−^{1}H COSY, HMBC, and NOESY spectra, compound **4** (neoabieslactone D) was thus established as (5*R*,17*S*,23*R*)-17,23-epoxy-3-oxolanosta-8,24-dien-26,23-olide.

Compound **5** was assigned the same molecular formula, $C_{30}H_{42}O_4$, as **4**, as shown by the negative HRESIMS at *m*/*z* 465.3032 $[M - H]^-$. The ^{1}H and ^{13}C NMR spectroscopic data were found to be almost the same for these two compounds, except that an olefinic bond could be located at the C-16,17 positions in **5**. This was supported by the absence of the ^{13}C NMR signals of C-16 (δ_C 37.3) and C-17 (δ_C 99.2) for **4**, while two sp^2 signals (δ_C 121.2 and 156.4) appeared for **5**. Further confirmation was found from the HMBC correlations of Me-18 (δ_H 0.77) with C-12, -13, -14, and -17 (δ_C 29.7, 51.3, 49.7, and 156.4). Comparison of the ^{1}H and ^{13}C NMR data of **5** with those of abiesanolide F suggested that they share the same side chain, which is a tautomeric mixture in the γ-lactone part.[15] This was coincident with the ^{13}C NMR spectroscopic characteristics of abiesanolide E as broad weak peaks for the side chain portion of the spectrum. On the basis of this evidence, compound **5** (neoabieslactone E) was therefore assigned as (5*R*)-23-hydroxy-3-oxolanosta-8,16,24-trien-26,23-olide.

Compound **6** exhibited a $[M - H]^-$ ion peak at *m*/*z* 467.3183 in the negative HRESIMS, corresponding to a molecular formula of $C_{30}H_{44}O_4$. The NMR data of **6** showed overall similarities to those of **5**, except for the presence of a hydroxy group (δ_C 76.7) at the C-3 position in **6** instead of a ketone moiety (δ_C 218.0) in **5**. In the NOESY spectrum, H-3 was correlated to H_3-19, which established a OH-3α group in **6**. Consequently, compound **6** (neoabieslactone F) was determined as (3*R*,5*R*)-3,23-dihydroxylanosta-8,16,24-trien-26,23-olide.

Seventeen known chemical constituents were also isolated from *Abies chensiensis*. By comparing the ^{1}H and ^{13}C NMR and MS data with those reported in the literature, these known compounds were identified as the triterpenoids cycloeucalenone[16] and cyclograndisolide;[17] the diterpenoids (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**7**),[18] 12-hydroxydehydroabietic acid,[19] abieta-7,13(14)-diene-18-oic acid,[20] torreferol,[21] 7-oxo-13α-hydroxyabiet-8(14)-en-18-oic acid,[22] manool (**8**),[23] abietinal,[24] (8α,12*Z*)-12,14-labdadien-8-ol,[25] 7α,18-dihydroxydehydroabietanol,[26] abiesadine N,[27] and 18-succinyloxyabieta-8,11,13-triene,[28] the norditerpenoids 8(14)-podocarpen-13-on-18-oic acid[29] and 8(14)-podocarpen-7,13-dion-18-oic acid,[29] and the monoterpenoids linalool[30] and oleuropeic acid.[31]

All 23 isolates were tested for inhibitory activities against LPS-induced NO production in RAW264.7 macrophages.[6] Neoabieslactone E (**5**), (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**7**), and manool (**8**) exhibited IC_{50} values of 9.1, 1.9, and 9.6 μg/mL, respectively. However, these three compounds were also somewhat cytotoxic (Table 3).

Experimental Section

General Experimental Procedures. Optical rotations were recorded using a Perkin-Elmer 341 polarimeter. UV spectra were obtained on a

Table 2. ^{13}C NMR Spectroscopic Data of Compounds **1**−**6** in $CDCl_3$

position	**1**[a]	**2**[a]	**3**[b]	**4**[b]	**5**[c]	**6**[d]
1	36.0 t	29.9 t	36.0 t	35.9 t	35.8 t	29.9 t
2	34.5 t	25.5 t	34.5 t	34.5 t	34.5 t	25.7 t
3	217.6 s	75.8 d	217.8 s	217.7 s	218.0 s	76.7 d
4	47.4 s	37.5 s	47.3 s	47.3 s	47.4 s	37.6 s
5	51.2 d	44.1 d	51.1 d	51.0 d	51.4 d	44.4 d
6	25.8 t	25.7 t	26.0 t	26.0 t	27.2 t	27.1 t
7	20.9 t	21.4 t	20.6 t	20.6 t	20.8 t	20.7 t
8	136.4 s	134.7 s	136.0 s	135.9 s	134.6 s	133.3 s
9	132.7 s	134.6 s	133.0 s	133.0 s	133.5 s	135.2 s
10	36.9 s	36.8 s	37.1 s	36.9 s	37.1 s	37.2 s
11	19.3 t	18.0 t	19.4 t	19.3 t	19.3 t	18.1 t
12	25.2 t	27.8 t	24.6 t	24.6 t	29.7 t	29.7 t
13	50.1 s	50.6 s	50.5 s	50.5 s	51.3 s	51.5 s
14	49.8 s	49.2 s	48.4 s	48.5 s	49.7 s	49.7 s
15	31.4 t	30.6 t	31.6 t	31.6 t	37.9 t	37.9 t
16	39.4 t	38.9 t	36.0 t	37.3 t	121.2 d	121.5 d
17	85.5 s	85.0 s	98.6 s	99.2 s	156.4 s	156.8 s
18	18.6 q	19.4 q	18.7 q	18.8 q	20.5 q	20.6 q
19	18.5 q	18.6 q	18.7 q	18.7 q	18.4 q	18.8 q
20	38.4 d	36.5 d	43.8 d	44.4 d	27.9 d	28.0 d
21	14.2 q	14.4 q	18.7 q	18.7 q	21.3 q	23.1 q
22	39.0 t	39.0 t	44.9 t	42.6 t	43.1 t	42.8 t
23	76.4 d	77.1 d	113.5 s	112.5 s	106.0 s	105.9 s
24	36.4 t	36.4 t	36.9 t	147.2 d	147.6 d	147.4 d
25	34.2 d	33.9 d	35.6 d	130.4 s	131.2 s	131.3 s
26	180.2 s	179.9 s	179.2 s	172.2 s	172.0 s	171.8 s
27	15.9 q	15.7 q	14.9 q	10.3 q	10.3 q	10.4 q
28	26.2 q	28.0 q	26.3 q	26.2 q	26.2 q	28.1 q
29	21.3 q	22.2 q	21.2 q	21.2 q	22.6 q	22.2 q
30	26.3 q	24.3 q	25.8 q	25.9 q	26.0 q	26.0 q

[a] Recorded at 150 MHz. [b] Recorded at 75 MHz. [c] Recorded at 125 MHz. [d] Recorded at 100 MHz.

Table 3. Inhibitory Effects of Compounds **5**, **7**, and **8** against LPS-Induced NO Production in RAW264.7 Macrophages and Their Cytotoxicity

	IC_{50} (μg/mL)	
compound	anti-inflammation[a]	cytotoxicity[b]
neoabieslactone E (**5**)	9.1	20.0
(12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**7**)	1.9	0.6
manool (**8**)	9.6	32.3
aminoguanidine[c]	3.4	not tested

[a] Inhibitory effects against LPS-induced NO production in RAW264.7 macrophages. [b] Cytotoxic effects on RAW264.7 macrophages. [c] Positive control.

Shimadzu UV-2550 spectrometer. IR spectra were recorded on a Bruker Vector 22 spectrometer with KBr pellets. NMR spectra were obtained on Bruker Avance 300, 400, 500, or 600 NMR spectrometers in $CDCl_3$ with TMS as internal standard. ESIMS were acquired on an Agilent LC/MSD Trap XCT mass spectrometer, whereas HRESIMS were measured using a Waters Q-TOF micro mass spectrometer. Materials for column chromatography were silica gel (100−200 mesh; Huiyou Silical Gel Development Co., Ltd., Yantai, People's Republic of China), Sephadex LH-20 (40−70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden), and YMC-Gel ODS-A (50 μm; YMC, Milford, MA). Preparative TLC (0.4−0.5 mm) was conducted with glass plates precoated with silica gel GF_{254} (Yantai). Compounds were visualized by exposure to UV light at 254 nm.

Plant Material. The aerial parts of *A. chensiensis* were collected from Jinqu, Baoji City, Shaanxi Province, in May 2007 and authenticated by Prof. Han-Ming Zhang in the Department of Pharmacognosy, Second Military Medical University. A voucher specimen (20070513002) was deposited at the Herbarium of School of Pharmacy, Second Military Medical University, Shanghai, People's Republic of China.

Extraction and Isolation. The air-dried and powdered aerial parts (17 kg) of *A. chensiensis* were extracted with 80% ethanol three times each for 3 h. On filtering, the extract was partitioned sequentially with $CHCl_3$ (20 L), EtOAc (40 L), and *n*-BuOH (30 L). The $CHCl_3$ extract was subjected to column chromatography over silica gel eluting with a gradient of petroleum ether−EtOAc (100 → 50%) to give three fractions (Fr.1−Fr.3). Fr.1 was chromatographed on silica gel with petrolum ether−EtOAc (50:1 → 20:1) to yield two subfractions (Fr.1A and Fr.1B). Fr.1A was purified by Sephadex LH-20 eluting with $CHCl_3$−MeOH (1:1) to give cyclograndisolide (20 mg), (12*R*,13*R*)-8,12-epoxy-14-labden-13-ol (**7**, 5 mg), 12-hydroxydehydroabietic acid (3 mg), and abieta-7,13(14)-diene-18-oic acid (9 mg). Fraction Fr.1B was chromatographed over Sephadex LH-20 eluting with $CHCl_3$−MeOH (1:1), followed by purification using preparative TLC to afford torreferol (23 mg), 7-oxo-13α-hydroxyabiet-8(14)-en-18-oic acid (4 mg), manool (**8**, 4 mg), abietinal (5 mg), (8α,12*Z*)-12,14-labdadien-8-ol (20 mg), 7α,18-dihydroxydehydroabietanol (47 mg), abiesadine N (23 mg), and 18-succinyloxyabieta-8,11,13-triene (10 mg). Fr.2 (60 g) was chromatographed on silica gel with $CHCl_3$−MeOH (50:1) to give two subfractions (Fr.2A and Fr.2B). Fr.2A was subjected to column chromatography on ODS (CH_3OH−H_2O, 70−100%) and then purified by Sephadex LH-20 eluting with MeOH to give neoabieslactone A (**1**, 50 mg), neoabieslactone B (**2**, 122 mg), neoabieslactone C (**3**, 7 mg), neoabieslactone D (**4**, 90 mg), neoabieslactone E (**5**, 20 mg), neoabieslactone F (**6**, 3.5 mg), and cycloeucalenone (10 mg). Fr.2B was chromatographed on Sephadex LH-20 to give linalool (4 mg), oleuropeic acid (34 mg), 8(14)-podocarpen-13-on-18-oic acid (15 mg), and 8(14)-podocarpen-7,13-dion-18-oic acid (3 mg).

Neoabieslactone A (1): needles; mp 188−190 °C; $[\alpha]^{20}_D$ +75.2 (*c* 0.30, MeOH); CD (MeOH) (nm) $\Delta\varepsilon_{223}$ −9.4, $\Delta\varepsilon_{255}$ +3.7; IR (KBr) ν_{max} 3510, 2958, 2935, 1751, 1695, 1460, 1383, 1189, 995 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (negative ion) *m/z* 469 $[M - H]^-$; HRESIMS (negative ion) *m/z* 469.3315 $[M - H]^-$ (calcd for $C_{30}H_{45}O_4$, 469.3318).

Neoabieslactone B (2): amorphous powder; $[\alpha]^{20}_D$ +26.7 (*c* 0.40, MeOH); CD (MeOH) (nm) $\Delta\varepsilon_{221}$ −7.5, $\Delta\varepsilon_{260}$ +4.6; IR (KBr) ν_{max} 3513, 2940, 2877, 1755, 1710, 1453, 1380, 1217, 1000 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (negative ion) *m/z* 507 $[M + Cl]^-$; HRESIMS (negative ion) *m/z* 507.3234 $[M + Cl]^-$ (calcd for $C_{30}H_{48}O_4Cl$, 507.3241); HRESIMS (positive ion) *m/z* 495.3463 $[M + Na]^+$ (calcd for $C_{30}H_{48}O_4Na$, 495.3450).

Neoabieslactone C (3): amorphous powder; $[\alpha]^{20}_D$ +7.0 (*c* 0.35, $CHCl_3$); CD (MeOH) (nm) $\Delta\varepsilon_{218}$ −8.0, $\Delta\varepsilon_{248}$ +4.9; IR (KBr) ν_{max} 3452, 2970, 1738, 1727, 1383, 1216, 910 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (positive ion) *m/z* 491 $[M + Na]^+$; HRESIMS (positive ion) *m/z* 491.3154 $[M + Na]^+$ (calcd for $C_{30}H_{43}O_4$, 491.3137).

Neoabieslactone D (4): needles; $[\alpha]^{20}_D$ −6.6 (*c* 0.50, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 212 (4.08) nm; CD (MeOH) (nm) $\Delta\varepsilon_{214}$ −12.3, $\Delta\varepsilon_{243}$ +4.0; IR (KBr) ν_{max} 3087, 2939, 1759, 1708, 1459, 1374, 1316, 1114, 957, 760 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (negative ion) *m/z* 465 $[M - H]^-$; HRESIMS (negative ion) *m/z* 465.2988 $[M - H]^-$ (calcd for $C_{30}H_{41}O_4$, 465.3005).

Neoabieslactone E (5): amorphous powder; $[\alpha]^{20}_D$ +16.0 (*c* 1.43, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 212 (4.92), 245 (4.30) nm; CD (MeOH) (nm) $\Delta\varepsilon_{224}$ −5.8, $\Delta\varepsilon_{248}$ +8.3; IR (KBr) ν_{max} 3419, 2917, 1754, 1700, 1437, 1207, 954, 705 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (negative ion) *m/z* 465 $[M - H]^-$; HRESIMS (negative ion) *m/z* 465.3032 $[M - H]^-$ (calcd for $C_{30}H_{41}O_4$,465.3005).

Neoabieslactone F (6): amorphous powder; $[\alpha]^{20}_D$ +11.7 (*c* 0.075, MeOH); UV (MeOH) λ_{max} (log ε) 210 (4.62), 284 (4.15) nm; CD (MeOH) (nm) $\Delta\varepsilon_{218}$ −10.2, $\Delta\varepsilon_{246}$ +5.1; IR (KBr) ν_{max} 3453, 2995, 2914, 1755, 1463, 1311, 1054, 954, 700 cm^{-1}; ^1H and ^{13}C NMR spectroscopic data, see Tables 1 and 2; ESIMS (negative ion) *m/z* 467 $[M - H]^-$; HRESIMS (negative ion) *m/z* 467.3183 $[M - H]^-$ (calcd for $C_{30}H_{43}O_4$, 467.3161).

X-ray crystallography of compound 1: needle crystal of $C_{30}H_{46}O_4$; space group $P2(1)2(1)2(1)$, a = 7.222(3) Å, α = 90°; b = 15.037(7) Å, β = 90°; c = 24.038(11) Å, γ = 90°; V = 2610(2) $Å^3$, Z = 4; crystal size 0.15 × 0.10 × 0.08 mm^3. A total of 4568 unique reflections (θ = 1.60−25.00°) were collected using graphite-monochromated Mo Kα (λ = 0.71073 Å) on a CCD area detector diffractometer. The structure was solved by direct methods (SHELXS-97) and expanded using Fourier techniques (SHELXS-97). The final cycle of full-matrix least-squares refinement was based on 4568 data, 0 restraints, and 307 variable parameters. Final R parameters indicated R_1 = 0.0566 and wR_2 = 0.1271 [$I > 2\sigma(I)$]. Crystallographic data (excluding structure factors) for neoabieslactone A (**1**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number

CCDC 713180. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Assays for Anti-inflammatory and Cytotoxic Activities. These two experiments were conducted according to a literature procedure.[6]

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Supporting Information Available: The 1D and 2D NMR spectra for compounds **1**−**6**. This information was available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Kuroyanagi, M.; Sugiyama, K.; Kanazawa, M.; Kawahara, N. *Chem. Pharm. Bull.* **2000**, *48*, 1917–1920.
(2) Yang, X. W.; Li, S. M.; Shen, Y. H.; Zhang, W. D. *Chem. Biodiversity* **2008**, *5*, 56–81.
(3) Gao, H. Y.; Wu, L. J.; Nakane, T.; Shirota, O.; Kuroyanagi, M. *Chem. Pharm. Bull.* **2008**, *56*, 554–558.
(4) Gao, H. Y.; Wu, L. J.; Nakane, T.; Shirota, O.; Kuroyanagi, M. *Chem. Pharm. Bull.* **2008**, *56*, 1352–1354.
(5) Sun, B. H.; Hou, B. L.; Huang, J.; Wu, L. J.; Kuroyanagi, M.; Gao, H. Y. *Arch. Pharm. Res.* **2008**, *31*, 1530–1533.
(6) 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*, 937–941.
(7) 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*, 4354–4362.
(8) 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**, *19*, 3042–3044.
(9) Zheng, W. J.; Fu, L. G. In *Flora of China*; Wu, Z. Y., Ed.; Science Press: Beijing, 1978; Vol. 7, pp 68−69.
(10) Li, Y. L.; Yang, X. W.; Zhang, W. D. *Biochem. Syst. Ecol.* **2008**, *36*, 932–934.
(11) Tanaka, R.; Wada, S. I.; Aoki, H.; Matsunaga, S.; Yamori, T. *Helv. Chim. Acta* **2004**, *87*, 240–249.
(12) Allen, F. H.; Kutney, J. P.; Trotter, J.; Westcott, N. D. *Tetrahedron Lett.* **1971**, 283–286.
(13) Hasegawa, S.; Kaneko, N.; Hirose, Y. *Phytochemistry* **1987**, *26*, 1095–1099.
(14) Ohira, T.; Yatagai, M. *Mokuzai Gakkaishi* **1992**, *38*, 180–185.
(15) Gao, H. Y.; Wu, L. J.; Nakane, T.; Shirota, O.; Kuroyanagi, M. *Chem. Pharm. Bull.* **2008**, *56*, 554–558.
(16) Khuong-Huu, F.; Sangare, M.; Chari, V. M.; Bekaert, A.; Devys, M.; Barbier, M.; Lukacs, G. *Tetrahedron Lett.* **1975**, 1787–1790.
(17) Kutney, J. P.; Grierson, D. S.; Knowles, G. D.; Westcott, N. D.; Rogers, I. H. *Tetrahedron* **1973**, *29*, 13–20.
(18) 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.
(19) Kinouchi, Y.; Ohtsu, H.; Tokuda, H.; Nishino, H.; Matsunaga, S. *J. Nat. Prod.* **2000**, *63*, 817–820.
(20) Lu, T.; Vargas, D.; Franzblau, S. G.; Fischer, N. H. *Phytochemistry* **1995**, *38*, 451–456.
(21) Shiojima, K.; Suzuki, M.; Aoki, H.; Ageta, H. *Chem. Pharm. Bull.* **1995**, *43*, 5–8.
(22) Zaidi, S. F. H.; Awale, S.; Kalauni, S. K.; Tezuka, Y.; Esumi, H.; Kadota, S. *Planta Med.* **2006**, *72*, 1231–1234.
(23) Ulubelen, A.; Topcu, G.; Eriş, C.; Sönmez, U.; Kartal, M.; Kurucu, S.; Bozok-Johansson, C. *Phytochemistry* **1994**, *36*, 971–974.
(24) San Feliciano, A.; Miguel del Corral, J. M.; Gordaliza, M.; Salinero, M. A. *Magn. Reson. Chem.* **1993**, *31*, 841–844.
(25) Barrero, A. F.; Altarejos, J. *Magn. Reson. Chem.* **1993**, *31*, 299–308.
(26) Ohmoto, T.; Kanatani, K.; Yamaguchi, K. *Chem. Pharm. Bull.* **1987**, *35*, 229–234.
(27) Yang, X. W. Chemical Constituents and Antitumor, Anti-inflammatory Activities of *Abies georgei* Orr and *Abies delavayi* Franch. Postdoctoral Thesis, Second Military Medical University, Shanghai, People's Republic of China, 2008; pp 40−41.
(28) Raldugin, V. A.; Grishko, V. V.; Kukina, T. P.; Druganov, A. G.; Druganov, A. G.; Shakirov, M. M. *Russ. Chem. Bull.* **2005**, *54*, 1747–1748.
(29) Cheung, H. T. A.; Miyase1, T.; Lenguyen, M. P.; Smal, M. A. *Tetrahedron* **1993**, *49*, 7903–7915.
(30) Bohlmann, F.; Zeisberg, R.; Klein, E. *Org. Magn. Reson.* **1975**, *7*, 426–432.
(31) Miyazawa, M.; Ohsawa, M. *J. Agric. Food Chem.* **2002**, *50*, 4916–4918.

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