Phenolic Compounds Isolated from the Bark of *Abies sachalinensis*

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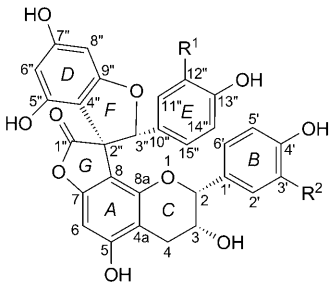
Eight spiro-biflavonoids named abiesinols A–H, along with three neolignans, quercetin, and protocatechuic acid were isolated from the MeOH extract of the bark of *Abies sachalinensis*. The structures of these phenolic compounds were characterized by spectroscopic methods including NMR and MS. The absolute configurations of the abiesinols were determined by *Mosher*'s method, CD, and NOESY data.

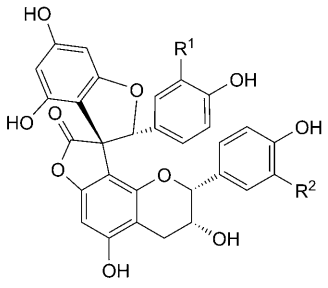
Introduction. – *Abies sachalinensis* (Japanese name: *Todomatsu*; Pinaceae) is a tall evergreen tree distributed in Hokkaido, Japan, and Sakhalin, Russia. As a part of our work on utilization of chemical constituents in the leaves and the barks of coniferous trees, which are considered to be waste products in the forest industry, we have investigated the barks of *A. sachalinensis* and *Picea jezoensis* var. *jezoensis*. We have previously isolated lanostane-type triterpenoids from the $CHCl_3$ extract of the bark of *A. sachalinensis*, and it was reported that these triterpenoids have DNA topoisomerase II inhibitory activities [1]. On a previous other study, we have described the isolation and structural elucidation of serratane-type triterpenoids from the $CHCl_3$ extract of *P. jezoensis* var. *jezoensis* and their antitumor-promoting activities [2–5]. Further examination of the MeOH extract of *P. jezoensis* var. *jezoensis* have shown the structures of flavonostilbenes named jezonocinols A–C and their radical-scavenging activities [6]. We have not researched the hydrophillic constituents from the bark of *A. sachalinensis* so far. Then, in the course of the isolation of the constituents from the MeOH extract of the bark of *A. sachalinensis*, eight spiro-biflavonoids named abiesinols A–H along with three neolignans, quercetin, and protocatechuic acid were isolated. In this article, we describe the isolation and the structural elucidation of phenolic compounds from *A. sachalinensis*, and the absolute configurations of abiesinols determined by *Mosher*'s method, CD, and NOESY data.

Results and Discussion. – The air-dried bark of *A. sachalinensis* was extracted successively with $CHCl_3$ and MeOH. The MeOH extract was separated by a combination of *Diaion HP-20*, normal-phase silica gel, *Sephadex LH-20* column chromatography, medium-pressure liquid chromatography (MPLC), and preparative TLC, followed by HPLC to afford eight spiro-biflavonoids, **1**–**8**, and one new *neo*-lignan (**9**) along with known compounds, dihydrodehydrodiconiferyl alcohol [7], cedrusin [8], quercetin [9], and protocatechuic acid [10] (*Fig. 1*).

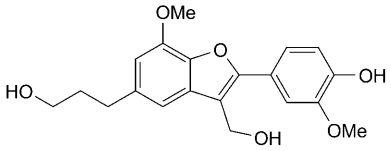
Abiesinol A (**1**) was obtained as a brown amorphous powder with a specific rotation of $[\alpha]_D^{19.9} = -110.2$. High-resolution secondary-ion MS (HR-SI-MS) analysis of **1**



	R^1	R^2
Abiesinol A (**1**)	H	OH
Abiesinol C (**3**)	OH	H
Abiesinol E (**5**)	H	H
Abiesinol G (**7**)	OH	OH



	R^1	R^2
Abiesinol B (**2**)	H	OH
Abiesinol D (**4**)	OH	H
Abiesinol F (**6**)	H	H
Abiesinol H (**8**)	OH	OH



9

Fig. 1. *Structures of phenolic compounds isolated from the bark of* Abies sachalinensis[1])

indicated the molecular formula of $C_{30}H_{22}O_{11}$, and the UV spectrum of **1** showed two absorption bands at 236.0 nm (log ε 4.16) and 277 nm (log ε 3.88). The IR spectrum displayed absorption bands at 3368 (OH), 1785 (γ-lactone CO), 1624, 1517, and 1469 cm^{-1} (aromatic ring). The aromatic region of the ^{1}H-NMR spectrum (*Table 1*) of **1** showed the presence of three sets of aromatic H-atoms corresponding to one 4-hydroxyphenyl group (δ(H) 7.06 (*d*, $J = 8.4$, 2 H), 6.63 (*d*, $J = 8.4$, 2 H)), one 3,4-dihydroxyphenyl group (δ(H) 6.82 (*d*, $J = 1.6$, 1 H), 6.78 (*d*, $J = 8.3$, 1 H), 6.53 (*dd*, $J =$ 8.3, 1.6, 1 H)), and one 2,4,6-tri-O-substituted phenyl group (δ(H) 6.09 (*d*, $J = 1.8$, 1 H), 6.01 (*d*, $J = 1.8$, 1 H). The spectrum further exhibited a set of one 3-hydroxy-2,8-(or 2,6)-disubstituted 5,7-di-O-substituted 3,4-dihydrobenzopyran (δ(H) 6.15 (*s*, H–C(6 or 8)[1])), 4.72 (*s*, H–C(2)), 4.16–4.18 (*m*, H–C(3)), 2.67 (*d*, $J = 3.7$, CH_2(4)). The ^{13}C-NMR spectrum (*Table 2*) of **1** showed signals for 30 C-atoms, whose correlations to H-atom signals were determined by 2D-NMR spectroscopic techniques (*Table 3*), and supported the above assignments. Analysis of the HMBC spectrum of **1** (*Fig. 2*, *Table 3*) gave the characteristic correlations between the H-atom signals at δ(H) 5.90 (*s*, H–C(3″)[1])) and the quaternary C-atom signal at δ(C) 179.2 (C(1″)) assignable to the γ-lactone CO signal and the spiro-center C-atom (C(2″)) at δ(C) 61.1. In addition, the *singlet* at δ(H) 5.90 (*s*, H–C(3″)) was correlated with the 4-hydroxyphenyl group C-atoms (C(10″), C(11″,15″)), and C(8) of the 3-hydroxy-2,8-disubstituted 5,7-di-O-substituted 3,4-dihydrobenzopyran. These characteristic HMBC patterns and the ^{1}H- and ^{13}C-NMR data of **1** were similar to those of larixinol [11][12]

[1]) Arbitrary atom numbering. For systematic names, see *Exper. Part.*

Table 1. *^{1}H-NMR Data for Abiesinols A–H* (**1**–**8**)[a])[1])

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
H–C(2)	4.72 (*s*)	4.98 (*s*)	4.90 (*s*)	5.00 (*s*)	4.81 (*s*)	5.00 (*s*)	4.82 (*s*)	4.96 (*s*)
H–C(3)	4.16–4.18 (*m*)	4.35 (br. *s*)	4.20 (br. *s*)	4.44 (br. *s*)	4.19 (br. *s*)	4.45 (br. *s*)	4.18 (br. *s*)	4.35 (br. *s*)
H_α–C(4)	2.67 (*d*, *J* = 3.7, 2 H)	2.91 (*dd*, *J* = 16.7, 3.9)	2.69 (*d*, *J* = 3.0, 2 H)	2.91 (*dd*, *J* = 17.0, 4.5)	2.67–2.70 (*m*, 2 H)	2.93 (*dd*, *J* = 16.7, 3.9)	2.67 (*d*, *J* = 3.6, 2 H)	2.90 (*dd*, *J* = 16.6, 4.3)
H_β–C(4)		2.94 (*dd*, *J* = 16.7, 3.9)		2.97 (*dd*, *J* = 17.0, 4.5)		2.98 (*dd*, *J* = 16.7, 3.9)		2.96 (*dd*, *J* = 16.6, 4.3)
H–C(6)	6.15 (*s*)	6.22 (*s*)	6.13 (*s*)	6.24 (*s*)	6.15 (*s*)	6.24 (*s*)	6.12 (*s*)	6.29 (*s*)
H–C(2′)	6.82 (*d*, *J* = 1.6)	6.96 (*d*, *J* = 1.5)	7.03 (*d*, *J* = 8.4)	7.22 (*d*, *J* = 8.6)	7.05 (*d*, *J* = 8.8)	7.28 (*d*, *J* = 7.8)	6.78 (*d*, *J* = 2.1)	6.95 (*d*, *J* = 1.9)
H–C(3′)			6.77 (*d*, *J* = 8.4)	6.78 (*d*, *J* = 8.6)	6.80 (*d*, *J* = 8.8)	6.77 (*d*, *J* = 7.8)		
H–C(5′)	6.78 (*d*, *J* = 8.3)	6.74 (*d*, *J* = 8.2)	6.77 (*d*, *J* = 8.4)	6.78 (*d*, *J* = 8.6)	6.80 (*d*, *J* = 8.8)	6.77 (*d*, *J* = 7.8)	6.74 (*d*, *J* = 8.1)	6.74 (*d*, *J* = 8.4)
H–C(6′)	6.53 (*dd*, *J* = 8.3, 1.6)	6.72 (*dd*, *J* = 8.2, 1.5)	7.03 (*d*, *J* = 8.4)	7.22 (*d*, *J* = 8.6)	7.05 (*d*, *J* = 8.8)	7.28 (*d*, *J* = 7.8)	6.47 (*dd*, *J* = 8.1, 2.1)	6.71 (*dd*, *J* = 8.4, 1.9)
H–C(3″)	5.90 (*s*)	6.35 (*s*)	5.82 (*s*)	6.28 (*s*)	5.89 (*s*)	6.33 (*s*)	5.82 (*s*)	6.23 (*s*)
H–C(6″)	6.01 (*d*, *J* = 1.8)	5.88 (*d*, *J* = 1.8)	6.01 (*d*, *J* = 1.8)	5.90 (*d*, *J* = 1.8)	6.02 (*d*, *J* = 2.1)	5.91 (*d*, *J* = 2.0)	5.99 (*d*, *J* = 1.8)	5.87 (*d*, *J* = 2.0)
H–C(8″)	6.09 (*d*, *J* = 1.8)	6.01 (*d*, *J* = 1.8)	6.05 (*d*, *J* = 1.8)	6.02 (*d*, *J* = 1.8)	6.07 (*d*, *J* = 2.1)	6.03 (*d*, *J* = 2.0)	6.06 (*d*, *J* = 1.8)	6.00 (*d*, *J* = 2.0)
H–C(11″)	7.06 (*d*, *J* = 8.4)	7.09 (*d*, *J* = 8.5)	6.77 (*d*, *J* = 1.6)	6.77 (*d*, *J* = 2.0)	7.05 (*d*, *J* = 8.5)	7.08 (*d*, *J* = 8.0)	6.77 (*d*, *J* = 1.8)	6.78 (*d*, *J* = 1.9)
H–C(12″)	6.63 (*d*, *J* = 8.4)	6.69 (*d*, *J* = 8.5)			6.63 (*d*, *J* = 8.5)	6.75 (*d*, *J* = 8.0)		
H–C(14″)	6.63 (*d*, *J* = 8.4)	6.69 (*d*, *J* = 8.5)	6.61 (*d*, *J* = 8.2)	6.72 (*d*, *J* = 8.4)	6.63 (*d*, *J* = 8.5)	6.75 (*d*, *J* = 8.0)	6.60 (*d*, *J* = 8.1)	6.72 (*d*, *J* = 8.4)
H–C(15″)	7.06 (*d*, *J* = 8.4)	7.09 (*d*, *J* = 8.5)	6.57 (*dd*, *J* = 8.2, 1.6)	6.57 (*dd*, *J* = 8.4, 2.0)	7.05 (*d*, *J* = 8.5)	7.08 (*d*, *J* = 8.0)	6.56 (*dd*, *J* = 8.1, 1.8)	6.59 (*dd*, *J* = 8.4, 1.9)

[a]) (D_6)Acetone solution; at 500 MHz; δ in ppm, *J* in Hz.

Table 2. *^{13}C-NMR Data for Abiesinols A–H* (**1**–**8**)[a])[1])

	1[b])	**2**[b])	**3**[b])	**4**[b])	**5**[b])	**6**[b])	**7**[b])	**8**[c])
C(2)	78.8	79.7	78.7	79.4	78.8	79.5	78.5	78.1
C(3)	66.4	65.9	66.4	65.4	66.4	65.4	66.3	63.7
C(4)	29.4	29.0	28.7	29.2	29.4	29.5	28.6	27.8
C(5)	157.3	157.7	157.3	157.6	157.4	157.8	156.9	156.5
C(6)	91.0	91.5	91.0	91.5	91.0	91.5	90.8	90.2
C(7)	152.2	153.6	152.2	153.5	152.3	153.5	151.9	151.6
C(8)	105.9	105.6	105.9	106.1	105.8	105.9	105.7	103.9
C(4a)	104.1	104.4	104.0	104.4	104.0	104.4	103.9	103.4
C(8a)	152.9	152.8	152.9	152.7	152.8	152.8	152.6	151.2
C(1′)	131.2	131.4	130.5	130.5	130.5	130.5	130.9	129.7
C(2′)	114.2	114.7	128.6	128.6	128.5	128.7	114.1	114.2
C(3′)	145.4	145.3	115.5	115.6	115.5	115.6	145.1	144.8
C(4′)	145.1	145.5	157.4	157.7	157.4	157.6	144.9	144.3
C(5′)	115.7	115.6	115.5	115.6	115.5	115.6	115.4	114.7
C(6′)	119.3	119.1	128.6	128.6	128.5	128.7	119.2	117.3
C(1″)	179.2	175.0	179.2	175.0	179.2	175.0	178.8	174.3
C(2″)	61.1	61.0	61.2	60.9	61.2	60.9	61.1	59.5
C(3″)	94.0	90.1	94.3	90.3	94.1	90.3	94.0	88.1
C(4″)	106.5	105.8	106.4	105.7	106.4	105.7	106.3	103.8
C(5″)	154.8	155.5	154.9	155.5	163.5	155.6	154.5	154.4
C(6″)	96.6	96.7	96.8	96.6	96.8	96.7	96.7	95.6
C(7″)	161.0	160.9	161.1	160.9	161.1	161.0	160.6	159.7
C(8″)	91.2	90.9	91.2	90.6	91.1	90.8	91.1	89.1
C(9″)	163.4	164.4	163.5	164.4	154.9	164.4	163.2	162.6
C(10″)	128.1	127.7	128.7	128.6	128.0	127.7	128.5	126.5
C(11″)	127.7	128.5	113.8	114.2	127.7	128.4	113.7	113.1
C(12″)	115.3	115.7	145.4	146.1	115.3	115.7	145.3	144.5
C(13″)	157.8	158.5	145.6	145.5	157.9	158.5	145.0	145.2
C(14″)	115.3	115.7	115.4	115.7	115.3	115.7	115.2	115.0
C(15″)	127.7	128.5	113.8	118.6	127.7	128.4	117.9	116.5

[a]) At 125 MHz; δ in ppm. [b]) In (D_6)acetone solution. [c]) In (D_6)DMSO.

and vitisinol [13], spiro-type biflavonoids isolated from *Larix gmelini* and *Vitis amurensis*, respectively. Therefore, based on these data, the planar structure of **1** was confirmed as shown in *Fig. 1*.

Abiesinol B (**2**) was obtained as a brown amorphous powder and was assigned the molecular formula, $C_{30}H_{22}O_{11}$, the same as **1**, by HR-SI-MS analysis. The UV and IR spectra of **2** also showed similar absorption bands (UV: 238, 276 nm; IR: 3398 br., 1791, 1624, 1516, 1466 cm^{-1}). The ^{1}H- and ^{13}C-NMR signals of **2** were closely related to those of **1**, except for the signals of C(1″)[1]) (δ(C) 179.2 (**1**), 175.0 (**2**)) and C(3″) (δ(H) 5.90 and δ(C) 94.0 (**1**); δ(H) 6.35 and δ(C) 90.1 (**2**)) (*Tables 1* and *2*). Furthermore, the analyses of the 2D-NMR spectra of **2** suggested the same planar structure as for **1** (*Fig. 2*, *Table 3*). The difference in the optical rotation and the retention time observed in HPLC of **1** and **2** indicated that **2** is a stereoisomer of **1**.

The relative configurations of C(2)/C(3)[1]) in both **1** and **2** were concluded to be of *cis*-epicatechin type from the characteristic feature of the H–C(2) signal in the

Table 3. *2D-NMR Correlation Data for Abiesinols A* (**1**) *and B* (**2**)[1])

	^{1}H,^{1}H-COSY		HMBC (H → C)		NOESY	
	1	**2**	**1**	**2**	**1**	**2**
H–C(2)	H–C(3)	H–C(3)	C(3), C(1′), C(2′), C(6′)	C(3), C(1′), C(2′), C(6′)	H–C(3), H–C(4), H–C(2′), H–C(6′), H–C(11″,15″), H–C(12″,14″)	H–C(3), H–C(2′,6′), H_β–C(4)
H–C(3)	H–C(2), H–C(4)	H–C(2), H–C(4)	C(2), C(4)	C(2), C(4)	H–C(4), H–C(11″,15″)	H_β–C(4)
H_α–C(4)	H–C(3)	H–C(3)	C(2), C(3), C(5), C(4a), C(8a)	C(2), C(3), C(5), C(4a), C(8a)	H–C(2), H–C(3)	
H_β–C(4)		H–C(3)				H–C(2), H–C(3)
H–C(6)			C(5), C(7), C(8), C(4a)	C(5), C(7), C(8), C(4a)		
H–C(2′)			C(6′)	C(2), C(6′)	H–C(2), H–C(6′)	H–C(3″)
H–C(5′)		H–C(6′)	C(1′), C(3′)	C(1′), C(3′)	H–C(6′), H–C(8″)	
H–C(6′)		H–C(5′)	C(2), C(2′)	C(2), C(6′)	H–C(2), H–C(5′), H–C(8″), H–C(11″,15″)	H–C(3″)
H–C(3″)			C(8), C(1″), C(2″), C(10″), C(11″,15″)	C(8), C(1″), C(2″), C(11″,15″)	H–C(11″,15″), H–C(12″,14″)	H–C(2′), H–C(6′), H–C(11″,15″)
H–C(6″)			C(4″), C(5″), C(7″), C(8″)	C(4″), C(5″), C(7″), C(8″)	H–C(8″)	
H–C(8″)			C(4″), C(6″), C(7″), C(9″)	C(4″), C(6″), C(7″), C(9″)	H–C(5′), H–C(6′), H–C(6″)	
H–C(11″,15″)	H–C(12″,14″)	H–C(12″,14″)	C(13″)	C(3″), C(13″)	H–C(2), H–C(3), H–C(3″), H–C(6′), H–C(12″,14″)	H–C(3″), H–C(12″,14″)
H–C(12″,14″)	H–(11″,15″)	H–C(11″,15″)	C(10″), C(13″)	C(10″), C(13″)	H–C(2), H–C(3), H–C(3″), H–C(11″,15″)	H–C(11″,15″)

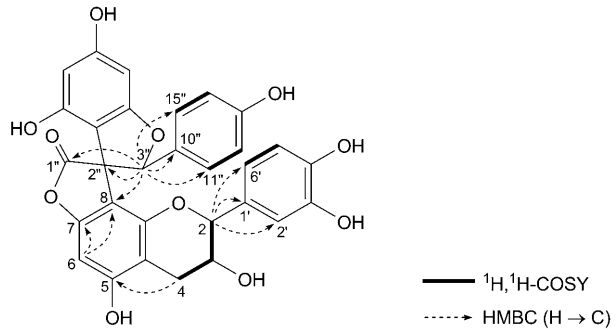


Fig. 2. *Diagnostic HMBC and ^{1}H,^{1}H-COSY correlations of abiesinols A* (**1**) *and B* (**2**)

^{1}H-NMR spectrum (δ(H) 4.72 (*s*, 1 H) (**1**); δ(H) 4.98 (*s*, 1 H) (**2**); *Table 1*) [14]. The spatial relationships in the molecules were deduced from the NOESY spectrum of **1** and **2** (*Fig. 3*, *Table 3*). In the NOESY spectrum of **1**, the correlations of H–C(8″) (*D* ring) with H–C(5′) and H–C(6′) (*B* ring), and of H–C(2) (*C* ring) with H–C(11″,15″) and H–C(12″,14″) (*E* ring) were observed and, while the NOESY spectrum of **2** did not show these correlations, however, the cross-peaks of H–C(3″) (*F* ring) with H–C(2′) and H–C(6′) (*B* ring) were observed. From these data, the relative relationships of C(2), C(3), C(2″), and C(3″) in **1** and **2** could be deduced as shown in *Fig. 3*, and the relation of **1** and **2** would be a stereoisomer at the C(2″), spiro-C-atom.

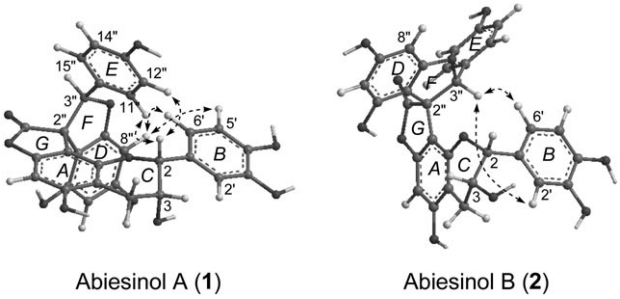


Fig. 3. *Configurations of abiesinols A* (**1**) *and B* (**2**) *and selected NOEs observed in the NOESY spectrum*

The absolute configuration of C(3)[1]) in **1** was determined by *Mosher*'s method on the (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) ester (**1a**) of the hexamethylether of **1** and the (*S*)-MTPA ester (**1b**) (*Fig. 4*) [15]. In the ^{1}H-NMR spectrum of **1a**, H–C(2), and H–C(2′), H–C(5′), and H–C(6′) (*B* ring) appeared downfield, whereas H–C(4) and H–C(6) were upfield in comparison to the same H-atoms of **1b**, indicating that in the (*S*)-MTPA ester, H–C(4) and H–C(6) were affected by the Ph ring of the MTPA moiety. Considering these and the aforementioned NOESY data, the absolute configurations at C(2), C(3), C(2″), and C(3″)[1]) in **1** were concluded to be all (*R*). The absolute configuration of **2** was determined by comparing the CD data with that of **1** (*Fig. 5*). The CD spectra of **1** and **2** showed *Cotton* effects of opposite signs around 205, 225, and 240 nm. Considering these data and the NOESY

data, the absolute configurations of C(2), C(3), C(2″), and C(3″) in **2** are (*R*), (*R*), (*S*), and (*R*), respectively.

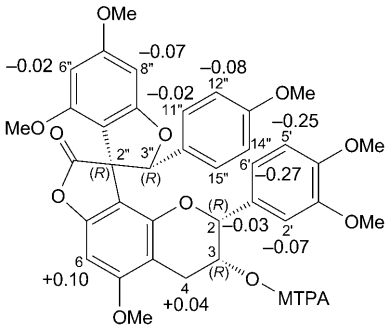


Fig. 4. *^{1}H-Chemical shift differences ($\Delta\delta = \delta_S - \delta_R$) between the* (R)- (**1a**) *and* (S)*-MTPA ester* (**1b**)

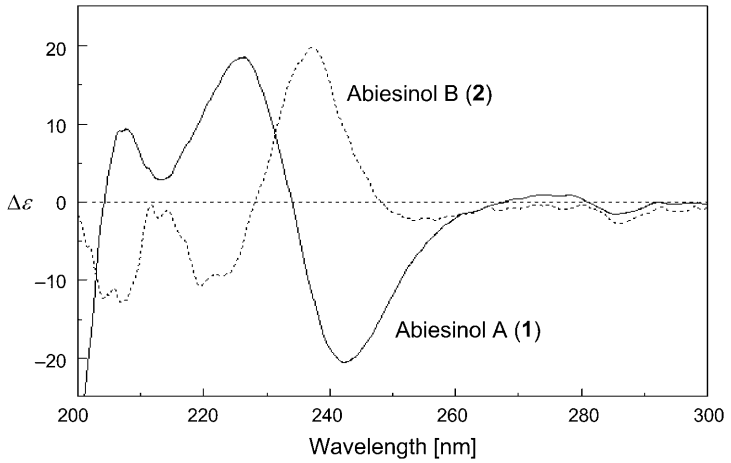


Fig. 5. *CD Spectra of abiesinols A* (**1**) (solid line) *and B* (**2**) (dotted line)

The NMR spectral data (*Tables 1* and *2*) indicated that the structures of **3**–**8** were similar to those of abiesinols A and B (**1** and **2**, resp.), and their molecular formulas were determined to be $C_{30}H_{22}O_{11}$ (**3** and **4**), $C_{30}H_{22}O_{10}$ (**5** and **6**), and $C_{30}H_{22}O_{12}$ (**7** and **8**). Furthermore, the ^{1}H-NMR spectra in the aromatic part of **3**–**8** suggested the presence of one 4-hydroxyphenyl group and one 3,4-dihydroxyphenyl group in **3** and **4**, two 4-hydroxyphenyl groups in **5** and **6**, and two 3,4-dihydroxyphenyl groups in **7** and **8**. The complete elucidation of the structures of **3**–**8** was achieved by 2D-NMR experiments. Consequently, compounds **3** and **4**, **5** and **6**, and **7** and **8** were found to have same planar structures as shown in *Fig. 1*, respectively. In addition, the similar optical rotations and CD curves of **3**, **5**, and **7** to those of **1**, and **4**, **6**, and **8** to **2** indicated that the absolute configurations of **3**, **5**, and **7** were same as that of **1**, and those of **4**, **6**, and **8** same as for **2**. Consequently, the configurations of **3**–**8** were determined as shown in *Fig. 1*, and named as abiesinols C–H. Compounds **5** and **7** were previously

isolated as larixinol from *Larix gmelini* [11][12], and vitisinol from *Vitis amurensis* [13], respectively. However, the absolute configurations of the compounds were not determined. In this article, we could describe the structural elucidations with the absolute configuration for the first time.

The spectroscopic data of **9** were similar to those of neolignans, dihydrodehydrodiconiferyl alcohol [7], and cedrusin [8], and the structure of **9** was identified as shown in *Fig. 1*. Although **9** was reported to be a synthetic derivative [16], so far as we know, **9** was isolated from a natural source for the first time.

The evaluation of the *in vitro* radical-scavenging activity and the *in vivo* antitumor-initiating activity on mouse skin tumors by the isolated phenolic compounds is now in progress.

Experimental Part

General. Column chromatography (CC): *Merck* Kieselgel *60* (SiO_2; 70–230 mesh), or *Sephadex LH-20*. MPLC: *Merck* Kieselgel *60* (230–400 mesh, *Merck*). Anal. TLC: *Merck* Kieselgel F_{254} (0.25 mm). Prep. TLC: *Merck* Kieselgel F_{254} (0.5 mm). HPLC: *Waters Delta 600*. Fractions obtained from CC were monitored by TLC and ^{1}H-NMR. Optical rotation: *Jasco DIP-1000* digital polarimeter. UV Spectra: *Hitachi U-2000* spectrophotometer; λ_{max} in nm; EtOH soln. CD Spectra: *Jasco J-500* spectropolarimeter; measured at r.t; EtOH soln. IR Spectra: *Jasco FT/IR-680 plus* spectrophotometer; KBr microplates; in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Varian INOVA 500* spectrometer; (D_6)acetone, (D_6)DMSO, and $CDCl_3$ solns.; δ in ppm rel. to Me_4Si (0 ppm) as an internal standard; coupling constants J in Hz. EI-MS, secondary-ion (SI)-MS, and FAB-MS: *Hitachi 4000 H* double-focusing mass spectrometer; in m/z.

Plant Material. The stem bark of *A. sachalinensis* was collected in the mountainous terrain under the control of National Hokkaido Bureau, Hidaka-cho, Japan, in September 2004. A voucher specimen (AS-0409) is deposited with the Herbarium of the Laboratory of Medicinal Chemistry, Osaka University of Pharmaceutical Sciences. The extraction was carried out in October 2004.

Extraction and Isolation. The chopped bark (13 kg) of *A. sachalinensis* was extracted successively with $CHCl_3$ (20 l × 3) and MeOH (20 l × 3) at r.t., and the solvents were concentrated to give the $CHCl_3$ (1.79 kg) and the MeOH (372 g) extracts. The MeOH extract was chromatographed on *Diaion HP-20* to give three fractions (*Fr. I* (78.2 g; MeOH/H_2O 1:1); *Fr. II* (103.5 g; MeOH/H_2O 3:1); *Fr. III* (172.3 g; MeOH). *Fr. I* was chromatographed on SiO_2 by gradient elution using $CHCl_3$ with increasing ratios of MeOH to give nine fractions (*Fr. I-A* (No. 1–7; 1.4 g), and *Fr. I-B* (No. 8–9; 0.9 g), $CHCl_3$ eluate; *Fr. I-C* (No. 10–14; 18.3 g), *Fr. I-D* (No. 15–24; 9.1 g), and *Fr. I-E* (No. 25–38; 6.3 g), $CHCl_3$/MeOH 10:1 eluate; *Fr. I-F* (No. 39–42; 9.3 g), *Fr. I-G* (No. 43–52; 12.5 g), and *Fr. I-H* (No. 53–58; 6.3 g), $CHCl_3$/MeOH 5:2 eluate; *Fr. I-I* (No. 59–62; 4.4 g), $CHCl_3$/MeOH 1:1 eluate). Further fractionation of *Fr. I-F* by a combination of MPLC (hexane/AcOEt, 1:2), *Sephadex LH-20* CC (MeOH), and HPLC (column *Xtera Prep MS C_{18} OBD* (*Waters*, 19 mm × 100 mm); MeOH/H_2O (27:73); flow rate, 8.53 ml/min; detection, UV 280 nm) gave abiesinols G (**7**) (23.7 mg) and H (**8**) (12.5 mg). Further purification with SiO_2 CC of *Frs. II* and *III* using a $CHCl_3$/MeOH gradient system (1:0–1:1) afforded 9 and 11 fractions, *Frs. II-A–IV-I* and *Frs. III-A–III-K*, resp. *Fr. II-C* (10.0 g) was fractionated on MPLC using $CHCl_3$/MeOH (50:1) followed by *Sephadex LH-20* (MeOH) to give quercetin (11.8 mg) [9] and protocatechuic acid (4.0 mg) [10]. *Fr. II-E* (10.7 g) was separated by MPLC using hexane/AcOEt (1:5) and *Sephadex LH-20* (MeOH), followed by HPLC (column *Xtera Prep MS C_{18} OBD* (*Waters*, 19 mm × 100 mm); MeOH/H_2O 27:73; flow rate, 8.53 ml/min; detection, UV 280 nm) to afford abiesinols A (**1**; 20.5 mg), B (**2**; 6.5 mg), C (**3**; 34.9 mg), D (**4**; 7.8 mg), E (**5**; 29.2 mg), and F (**6**; 7.3 mg). Further purification of *Fr. III-B* (10.5 g) by a combination of MPLC ($CHCl_3$/AcOEt 1:2), *Sephadex LH-20* CC (MeOH), and preparative TLC (hexane/AcOEt 1:9) gave **9** (3.1 mg), dihydrodehydrodiconiferyl alcohol (6.4 mg) [7], and cedrusin (21.3 mg) [8].

Abiesinol A (=*(2*R,*2′*R,*3*R,*3′*R*)-2′-(3,4-Dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2-(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **1**). Brown amorphous powder. $[\alpha]_D^{19.9} = -110.2$ ($c = 1.02$, MeOH). UV: 236.0 (4.16), 277.0 (3.88). CD ($c = 7.35 \times 10^{-5}$ M): +18.5 (227), −20.5 (242). IR: 3368 (br., OH), 1785 (γ-lactone C=O), 1624, 1517, 1469 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. ESI-MS: 559 (6.6), 407 (2.1), 379 (2.2), 23 (12.0), 207 (41.7), 131 (11.8), 115 (100). HR-SI-MS: 559.1244 ($[M+H]^+$, $C_{30}H_{23}O_{11}^+$; calc. 559.1240).

Abiesinol B (=*(2*R,*2′*R,*3*S,*3′*R*)-2′-(3,4-Dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2-(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **2**). Brown amorphous powder. $[\alpha]_D^{17.4} = -25.6$ ($c = 0.32$, MeOH). UV: 238.0 (4.01), 276.0 (3.67). CD ($c = 3.76 \times 10^{-5}$ M): −10.9 (223), +19.8 (237). IR: 3398 (br., OH), 1791 (γ-lactone C=O), 1624, 1516, 1466 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. SI-MS: 559 (1.3), 391 (1.1), 299 (2.2), 207 (30.4), 115 (100). HR-SI-MS: 559.1233 ($[M+H]^+$, $C_{30}H_{23}O_{11}^+$; calc. 559.1240).

Abiesinol C (=*(2*R,*2′*R,*3*R,*3′*R*)-2-(3,4-Dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2′-(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **3**). Brown amorphous powder. $[\alpha]_D^{19.1} = -142.0$ ($c = 0.74$, MeOH). UV: 238.5 (3.71), 273.5 (3.65). CD ($c = 3.76 \times 10^{-5}$ M): +14.3 (231), −20.7 (246). IR: 3359 (br., OH), 1785 (γ-lactone C=O), 1623, 1516, 1469 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. SI-MS: 559 (5.7), 391 (3.0), 299 (6.9), 223 (9.9), 207 (44.5), 131 (7.7), 115 (100). HR-SI-MS: 559.1243 ($[M+H]^+$, $C_{30}H_{23}O_{11}^+$; calc. 559.1240).

Abiesinol D (=*(2*R,*2′*R,*3*S,*3′*R*)-2-(3,4-Dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2′-(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **4**). Brown amorphous powder. $[\alpha]_D^{18.6} = -15.9$ ($c = 0.51$, MeOH). UV: 238.5 (3.87), 276.5 (3.70). CD ($c = 4.67 \times 10^{-5}$ M): −5.0 (231), +3.0 (241). IR: 3399 (br., OH), 1786 (γ-lactone C=O), 1627, 1517, 1467 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. SI-MS: 559 (4.7), 391 (3.2), 299 (6.6), 207 (40.2), 133 (10.7), 131 (4.7), 115 (100). HR-ESI-MS: 559.1236 ($[M+H]^+$, $C_{30}H_{23}O_{11}^+$; calc. 559.1240).

Abiesinol E (=*(2*R,*2′*R,*3*R,*3′*R*)-3′,4′-Dihydro-3′,4,5′,6-tetrahydroxy-2,2′-bis(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **5**). Brown amorphous powder. $[\alpha]_D^{19.9} = -112.0$ ($c = 0.59$, MeOH). UV: 239.0 (3.73), 272.0 (3.54). CD ($c = 6.73 \times 10^{-5}$ M): +4.3 (226), −4.3 (242). IR: 3312 (br., OH), 1785 (γ-lactone C=O), 1624, 1517, 1471 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. SI-MS: 543 (9.0), 497 (3.3), 299 (5.1), 207 (30.9), 115 (100). HR-SI-MS: 543.1295 ($[M+H]^+$, $C_{30}H_{23}O_{10}^+$; calc. 543.1291).

Abiesinol F (=*(2*R,*2′*R,*3*S,*3′*R*)-3′,4′-Dihydro-3′,4,5′,6-tetrahydroxy-2,2′-bis(4-hydroxyphenyl)-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **6**). Brown amorphous powder. $[\alpha]_D^{19.3} = -17.3$ ($c = 0.46$, MeOH). UV: 234.0 (4.19), 272.5 (3.67). CD ($c = 8.39 \times 10^{-5}$ M): −6.0 (220), +15.0 (236). IR: 3375 (br., OH), 1789 (γ-lactone C=O), 1626, 1517, 1468 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. SI-MS: 543 (4.9), 391 (6.7), 299 (9.4), 207 (62.0), 115 (100). HR-SI-MS: 543.1295 ($[M+H]^+$, $C_{30}H_{23}O_{10}^+$; calc. 543.1291).

Abiesinol G (=*(2*R,*2′*R,*3*R,*3′*R*)-2,2′-Bis(3,4-dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **7**). Brown amorphous powder. $[\alpha]_D^{24.0} = -106.1$ ($c = 0.52$, MeOH). UV: 238.5 (3.72), 279.5 (3.49). CD ($c = 8.28 \times 10^{-5}$ M): +3.3 (231), −10.6 (245). IR: 3375 (br., OH), 1785 (γ-lactone C=O), 1624, 1521, 1472 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. FAB-MS: 575 (19.4), 497 (8.6), 391 (8.3), 299 (10.7), 207 (73.8), 115 (100). HR-FAB-MS: 575.1192 ($[M+H]^+$, $C_{30}H_{23}O_{12}^+$; calc. 575.1190).

Abiesinol H (=*(2*R,*2′*R,*3*S,*3′*R*)-2,2′-Bis(3,4-dihydroxyphenyl)-3′,4′-dihydro-3′,4,5′,6-tetrahydroxy-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-8′-one*; **8**). Brown amorphous powder. $[\alpha]_D^{24.0} = -17.7$ ($c = 0.33$, MeOH). UV: 237.0 (3.94), 279.5 (3.62). CD ($c = 5.51 \times 10^{-5}$ M): −1.3 (231), +4.2 (244). IR: 3409 (br., OH), 1792 (γ-lactone C=O), 1628, 1521, 1465 (arom. ring). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. FAB-MS: 575 (2.4), 497 (2.7), 391 (3.5), 299 (5.9), 207 (52.2), 115 (100). HR-FAB-MS: 575.1192 ($[M+H]^+$, $C_{30}H_{23}O_{12}^+$; calc. 575.1190).

4-[3-(Hydroxymethyl)-5-(3-hydroxypropyl)-7-methoxy-1-benzofuran-2-yl]-2-methoxyphenol (**9**). Pale yellow amorphous powder. UV: 232.5 (3.83), 286.0 (3.78), 294.0 (3.78). IR: 3393 (br., OH), 1601, 516, 1487 (arom. ring). ^{1}H-NMR ((D$_6$)acetone): 7.55 (*d*, $J = 1.9$, H−C(2)); 7.42 (*dd*, $J = 8.3$, 1.9, H−C(6)); 7.14 (*d*, $J = 1.5$, H−C(6′)); 6.98 (*d*, $J = 8.3$, H−C(5)); 6.79 (*d*, $J = 1.5$, H−C(2′)); 4.85 (*d*, $J = 5.3$, CH$_2$(9)); 4.01 (*s*, MeO−C(3)); 3.95 (*s*, MeO−C(3′)); 3.58–3.63 (*m*, CH$_2$(9′)); 2.77–2.80 (*m*, CH$_2$(7′));

1.86–1.91 (*m*, CH_2(8′)). ^{13}C-NMR: ((D$_6$)acetone): 161.6 (*s*, C(3)); 154.8 (*s*, C(7)); 148.4 (*s*, C(4)); 145.8 (*s*, C(3′)); 140.1 (*s*, C(4′)); 138.9 (*s*, C(1′)); 124.7 (*s*, C(5′)); 123.3 (*s*, C(1)); 121.5 (*d*, C(6)); 116.2 (*d*, C(5)); 115.4 (*s*, C(8)); 112.0 (*d*, C(6′)); 111.6 (*d*, C(2)); 108.5 (*d*, C(2′)); 61.8 (*t*, C(9′)); 56.4 (*q*, *Me*O–C(3)); 56.3 (*q*, *Me*O–C(3′)); 55.2 (*t*, C(9)); 36.1 (*t*, C(8′)); 33.3 (*t*, C(7′)). SI-MS: 381 (6.4), 358 (39.0), 341 (100), 309 (7.8), 207 (14.1), 151 (8.4), 115 (80.3). HR-SI-MS: 381.1315 ($[M+Na]^+$, $C_{20}H_{22}NaO_6^+$; calc. 381.1314).

Synthesis of the MTPA Esters **1a** *and* **1b**. A mixture of **1** (5.0 mg) and diazomethane in MeOH/Et_2O (1:1, 4 ml) was stirred for 24 h. The mixture was concentrated to give hexamethylabiesinol A (3.3 mg). To a stirred soln. of the hexamethylether derivative (1.0 mg) in dry pyridine (0.2 ml) and (+)-(*R*)-MTPA chloride or (−)-(*S*)-MTPA chloride (20 µl) was added. The mixture was stirred overnight at 80° and subjected to preparative TLC with hexane/AcOEt (1:1) to afford the (*R*)-MTPA ester (**1a**, 1.0 mg) or the (*S*)-MTPA ester (**1b**, 1.2 mg).

*(*R*)-MTPA Ester* (= *(2*R*,2′*R*,3*R*,3′*R*)-3′,4′-Dihydro-2′-(3,4-dimethoxyphenyl)-4,5′,6-trimethoxy-2-(4-methoxyphenyl)-8′-oxo-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-3′-yl (2*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate*; **1a**). White amorphous powder. ^{1}H-NMR ((D$_6$)DMSO): 7.39 (*t*, *J* = 7.0, 1 arom. H of MTPA); 7.21 (*t*, *J* = 7.8, 2 arom. H of MTPA); 7.02 (*d*, *J* = 8.7, H–C(11″)[1]), H–C(15″)); 6.90 (*d*, *J* = 8.0, 2 arom. H of MTPA); 6.90 (*d*, *J* = 2.0, H–C(2′)); 6.84 (*d*, *J* = 8.5, H–C(5′)); 6.79 (*d*, *J* = 8.7, H–C(12″), H–C(14″)); 6.64 (*dd*, *J* = 8.5, 2.0, H–C(6′)); 6.47 (*s*, H–C(6)); 6.33 (*d*, *J* = 1.9, H–C(8″)); 6.09 (*d*, *J* = 1.9, H–C(6″)); 5.90 (*s*, H–C(3″)); 5.59 (*s*, H–C(3)); 4.95 (*s*, H–C(2)); 3.81 (*s*, MeO); 3.78 (*s*, MeO); 3.71 (*s*, MeO); 3.68 (*s*, MeO); 3.64 (*s*, MeO); 3.40 (*s*, MeO); 2.99 (*s*, MeO); 2.83 (*dd*, *J* = 17.4, 4.3, H_β–C(4)); 2.70 (br. *d*, *J* = 17.4, H_α–C(4)). EI-MS: 858 (100), 830 (75.7), 624 (14.5), 596 (43.8), 434 (37.8), 419 (11.4), 189 (38.4), 151 (16.2), 57 (9.0), 43 (6.56).

*(*S*)-MTPA Ester* (= *(2*R*,2′*R*,3*R*,3′*R*)-3′,4′-Dihydro-2′-(3,4-dimethoxyphenyl)-4,5′,6-trimethoxy-2-(4-methoxyphenyl)-8′-oxo-2′*H*-spiro[1-benzofuran-3,9′-furo[2,3-*h*]chromen]-3′-yl (2*S*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate*; **1b**). White amorphous powder. ^{1}H-NMR ((D$_6$)DMSO): 7.39 (*t*, *J* = 7.0, 1 arom. H of MTPA); 7.17 (*t*, *J* = 8.0, 2 arom. H of MTPA); 7.00 (*d*, *J* = 8.7, H–C(11″)[1]), H–C(15″)); 6.83 (*d*, *J* = 1.8, H–C(2′)); 6.83 (*d*, *J* = 8.5, 2 arom. H of MTPA); 6.71 (*d*, *J* = 8.7, H–C(12″), H–C(14″)); 6.59 (*d*, *J* = 8.5, H–C(5′)); 6.56 (*s*, H–C(6)); 6.37 (*dd*, *J* = 8.5, 1.8, H–C(6′)); 6.26 (*d*, *J* = 2.0, H–C(8″)); 6.07 (*d*, *J* = 2.0, H–C(6″)); 5.90 (*s*, H–C(3″)); 5.57 (br. *s*, H–C(3)); 4.92 (*s*, H–C(2)); 3.77 (*s*, MeO); 3.74 (*s*, MeO); 3.74 (*s*, MeO); 3.67 (*s*, MeO); 3.59 (*s*, MeO); 3.45 (*s*, MeO); 2.87 (*dd*, *J* = 17.5, 4.5, H_β–C(4)); 2.85 (*s*, MeO); 2.70 (br. *d*, *J* = 17.5, H_α–C(4)). EI-MS: 858 (100), 830 (68.9), 624 (14.1), 596 (44.0), 434 (43.7), 419 (13.4), 189 (62.4), 151 (23.1), 57 (16.1), 43 (15.9).

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Received January 29, 2009