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FLAVONOIDS AND LIGNANS FROM LEAVES OF *CRYPTOMERIA JAPONICA*

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Key Word Index—*Cryptomeria japonica*; Taxodiaceae; leaves; flavonoids; lignans.

Abstract—Eight flavonoids and 10 lignans were isolated from the leaves of *Cryptomeria japonica*. The new compounds are *cis*-dihydrodehydrodiconiferyl alcohol triacetate and *seco*dihydrodehydrodiconiferyl alcohol tetraacetate. Their structures were determined by chemical and spectral methods.

INTRODUCTION

The Japanese cedar, *Cryptomeria japonica*, is a widely distributed conifer called 'sugi' in Japanese. We recently reported the isolation of sesquiterpenes [1], diterpenes of abietane-, kaurane- and labdane-types [2, 3], and a triterpene, chamaecydin [4], from the ethyl acetate-soluble part of its leaves. We describe herein 18 constituents comprised of flavonoids and lignans, including two novel compounds **16** and **17**.

RESULTS AND DISCUSSION

The leaves of *C. japonica* were extracted with acetone. The ethyl acetate-soluble portion of the extract was chromatographed to give flavonoids and lignans **1**–**18**. The known flavonoids, taxifolin (**1**) [5], 5-hydroxy-4′,7-dimethoxyflavone (**2**) [6], 5-hydroxy-3,4′,7-trimethoxyflavone (**3**) [7], 5-hydroxy-3,3′,4′,7-tetramethoxyflavone (**4**) [8], quercetin (**5**) [9], catechol pentaacetate (**6**) [10], epicatechol pentaacetate (**7**) [10] and 4′,4‴,7,7″-tetramethylamentoflavone (**8**) [11], the known lignans, matairesinol (**9**) [12], nortrachelogenin (**10**) [13], isolariciresinol tetraacetate (**11**) [14], secoisolariciresinol tetraacetate (**12**) [14], cedrusinin triacetate (**13**) [15], dihydrodehydrodiconiferyl alcohol triacetate (**14**) [16], cedrusin tetraacetate (**15**) [16] and agatharesinol tetraacetate (**18**) [17], were identified by comparison of their physical and spectral data (mp, $[\alpha]$, mass, IR, ^{1}H and ^{13}C NMR) with literature data.

Compound **16** ($C_{26}H_{30}O_9$) was assigned as *cis*-dihydrodehydrodiconiferyl alcohol triacetate because it showed characteristic IR and NMR spectra (Table 1) similar to those of the *trans*-isomer **14**. The *cis*-configuration of **16** was established by irradiation of H-7 (at δ5.82) which caused a 6.5% nOe of H-8 (at δ3.80). Due to the shielding effects of the adjacent groups, the C-9 protons (at δ3.82 and 3.92) and the C-9-OAc (at δ1.81) of **16** appeared at higher fields than those of *trans*-isomer **14**, occurring at δ4.22, 4.38 and 2.05. The CD spectrum of **16** is similar to that of **14**, exhibiting a negative Cotton effect at 276.5 nm and a positive Cotton effect at 253 nm. Accordingly, compound **16** has the (7*S*,8*S*)-configuration.

Compound **17** ($C_{28}H_{34}O_{10}$) showed IR absorptions at 1756 and 1730 cm^{-1} and ^{13}C signals at δ168.8, 168.9, 169.1 and 171.0 attributable to four acetoxy groups. By analysis of the ^{1}H, ^{13}C and H–C correlated spectra, the structure of **17** was determined to be *seco*dihydrodehydrodiconiferyl alcohol tetraacetate. Compound **17** was correlated with **14** by a sequence of hydrogenolysis, giving a tetraol **17a**, and acetylation (Scheme 1). This correlation confirms that **17** has the 8*S*-configuration. Its CD spectrum showed a negative Cotton effect at 286.5 nm and a positive Cotton effect at 264.5 nm.

EXPERIMENTAL

General. Merck silica gel 60F sheets were used for analytical TLC. HPLC was carried out on a Hibar Lichrosorb Si 60 (7 μm or 10 μm) column (25 cm × 1 cm).

Plant material. The plant used in this study was introduced from Japan and cultivated in suburban Taipei. A voucher specimen is deposited in our laboratory. Leaves (1.4 kg) of *C. japonica* D. Don. were exhaustively extracted with Me_2CO. The Me_2CO extract was passed through a pad of charcoal, concd and re-extracted with EtOAc. The EtOAc-sol. portion (45 g) was chromatographed on a silica gel column, eluting with gradients of hexane and EtOAc. Appropriate frs were comb. and purified by HPLC to give **18** (13 mg), **13** (4 mg), **15** (9 mg), **16** (8 mg), **14** (110 mg), **3** (10 mg), **2** (55 mg), **4** (12 mg), **12**

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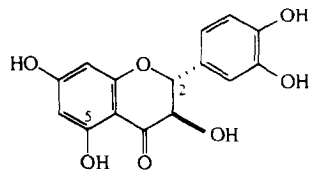

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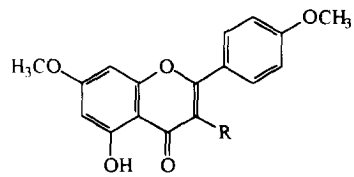

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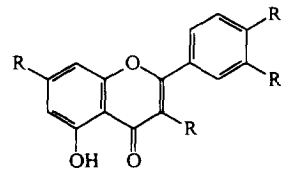
3 R = OCH_3



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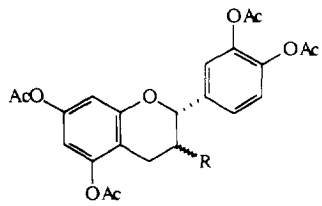
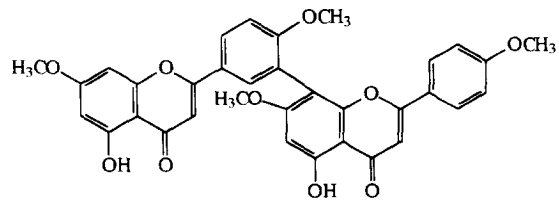
5 R = OH



6 R = β-OAc
7 R = α-OAc



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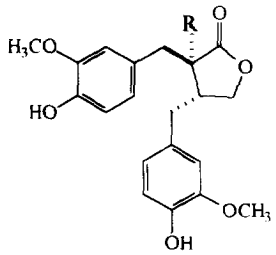

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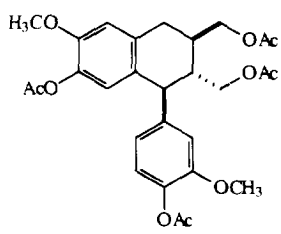
10 R = OH



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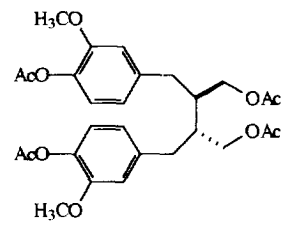

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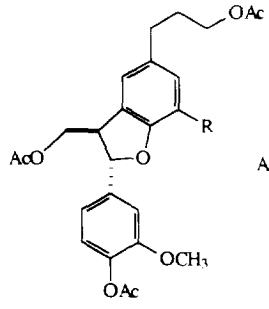
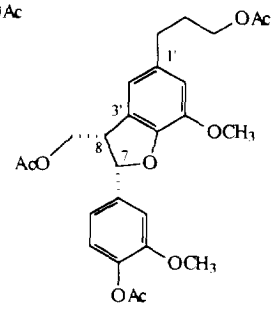


13 R = H
14 R = OCH_3
15 R = OAc



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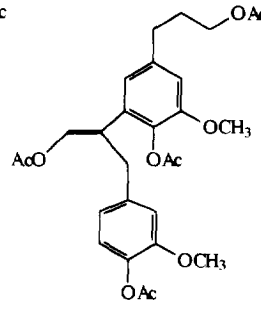

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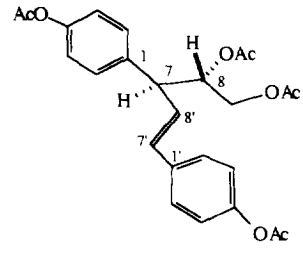


18

(17 mg), **17** (20 mg), **6** (13 mg), **7** (15 mg), **11** (15 mg), **8** (14 mg), **9** (15 mg), **10** (12 mg), **5** (10 mg) and **1** (15 mg), in order of increasing polarity, respectively.

Cedrusinin triacetae (**13**). ^{13}C NMR ($CDCl_3$, 75 MHz): δ30.6 (C-8′), 31.6 (C-7′), 50.4 (C-8), 56.0 (OMe), 63.7 (C-9′), 65.7 (C-9), 87.0 (C-7), 109.5 (C-5′), 109.7 (C-2), 118.0 (C-6), 122.9 (C-5), 124.6 (C-6′), 126.0 (C-1′), 129.2 (C-2′), 134.0 (C-3′), 139.5 (C-4), 140.1 (C-1), 151.3 (C-3), 158.0 (C-4′), 20.6, 20.8, 21.0, 168.9, 170.8, 171.1 (3 × OAc).

Cedrusin tetraacetate (**15**). ^{13}C NMR ($CDCl_3$, 75 MHz): δ30.3 (C-8′), 31.5 (C-7′), 51.1 (C-8), 56.0 (OMe), 63.7 (C-9′), 65.5 (C-9), 87.9 (C-7), 109.6 (C-2), 117.5 (C-6),

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **16** and **17** ($CDCl_3$ solution, δ, J values in Hz)

	δ_H (300 MHz)		δ_C (75 MHz)	
	16	**17**	**16**	**17**
1	—	—	139.5	138.0
2	7.01 (*d*, *J*2)	6.60 (*d*, *J*2)	110.6	113.2
3	—	—	151.1	150.6
4	—	—	139.3	138.2
5	7.0 (*d*, *J*8)	6.85 (*d*, *J*8)	122.6	122.4
6	6.95 (*dd*, *J*2, 8)	6.64 (*dd*, *J*2, 8)	118.8	121.0
7	5.82 (*d*, *J*7.5)	2.86 (*dd*, *J*7, 11)	86.5	37.9
		2.90 (*dd*, *J*7, 11)		
8	3.80 (*ddd*, *J*3, 6, 7.5)	3.44 (*dddd*, *J*7, 7, 7, 7)	46.0	39.2
9	3.82 (*dd*, *J*6, 11.5)	4.16 (*dd*, *J*7, 10.5)	63.6	66.4
	3.92 (*dd*, *J*3, 11.5)	4.22 (*dd*, *J*7, 10.5)		
1′	—	—	128.6	139.6
2′	6.66 (*d*, *J*2)	6.54 (*d*, *J*2)	117.1	119.2
3′	—	—	135.4	134.1
4′	—	—	146.2	136.5
5′			144.2	151.0
6′	6.64 (*d*, *J*2)	6.62 (*d*, *J*2)	113.0	110.7
7′	2.62 (*t*, *J*7)	2.59 (*t*, *J*7)	32.0	32.3
8′	1.92 (*tt*, *J*6.5, 7)	1.87 (*tt*, *J*6.5, 7)	30.6	30.2
9′	4.08 (*t*, *J* 6.5)	4.05 (*t*, *J*6.5)	63.7	63.7
OMe	3.80 (*s*)	3.69 (*s*)	56.0	55.7
	3.89 (*s*)	3.77 (*s*)	56.2	55.9
OAc	1.81 (*s*)	1.94 (*s*)	20.5, 168.8	20.5, 168.8
	2.05 (*s*)	2.05 (*s*)	20.6, 170.5	20.6, 168.9
	2.28 (*s*)	2.25 (*s*)	21.0, 171.1	20.8, 169.1
		2.29 (*s*)		20.9, 171.0

Assignments of ^{1}H and ^{13}C resonances confirmed by H–C COSY and HMBC spectra, as well as by NOE experiments.

122.1 (C-6′), 122.4 (C-2′), 122.8 (C-5), 128.0 (C-1′), 133.8 (C-5′), 135.0 (C-3′), 139.5 (C-4), 139.8 (C-1), 149.0 (C-4′), 151.4 (C-3), 20.2, 20.6, 20.8, 20.9, 168.9, 170.6, 170.7, 171.1 (4 × OAc).

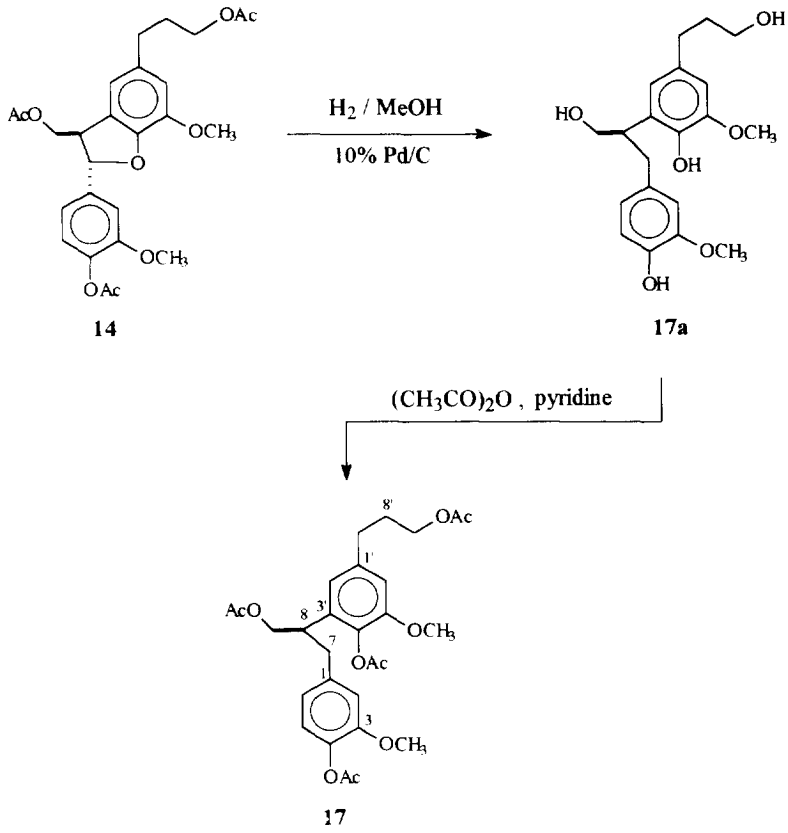
Cis-*Dihydrodehydrodiconiferyl alcohol triaacetate* (**16**). Gum. $[\alpha]_D^{25}$ −66° ($CHCl_3$; *c* 0.8). TLC (EtOAc–CH_2Cl_2, 1:9), R_f 0.48. IR ν_{max}^{neat} cm^{-1}: 1757, 1728, 1601, 1494. UV λ_{max}^{MeOH} nm (ε): 281 (5550), 255 (1700), 211 (40250). CD (MeOH): $[\theta]_{318}$ + 670, $[\theta]_{276.5}$ −2240, $[\theta]_{253}$ + 2700. EIMS (70 eV) *m/z* (rel. int.) 486 $[M]^+$ (4), 426 (5), 384 (25), 369 (5), 265 (6), 165 (10), 43 (100). HRMS for $C_{26}H_{30}O_9$, requires 486.1890; found $[M]^+$ *m/z* 486.1892.

seco*Dihydrodehydrodiconiferyl alcohol tetraacetate* (**17**). Gum. $[\alpha]_D^{25}$ − 2.5° ($CHCl_3$; *c* 2.0). TLC (EtOAc–$CHCl_3$–hexane, 1:1:1) R_f 0.75. IR ν_{max}^{neat} cm^{-1}: 1756, 1730, 1593, 1505. UV λ_{max}^{MeOH} nm (ε): 274 (7700). CD (MeOH): $[\theta]_{264.5}$ + 670, $[\theta]_{286.5}$ − 550. EIMS (70 eV) *m/z* (rel. int.) 530 $[M]^+$ (12), 488 (75), 446 (25), 428 (60), 386 (42), 189 (65), 137 (90), 43 (100). HRMS for $C_{28}H_{34}O_{10}$, requires 530.2152; found $[M]^+$ *m/z* 530.2153.

Correlation of **17** *with* **14**. A mixt. of **14** (20 mg) and 10% Pd/C (5 mg) in MeOH (5 ml) was stirred at 20° under an H_2 atmosphere for 16 hr. The mixt. was filtered, the filtrate concd and purified by HPLC and elution with EtOAc–hexane (4:1) to give *seco*lignan **17a** (18 mg). Gum. $[\alpha]_D^{25}$ + 39° ($CHCl_3$; *c* 1.5). TLC (EtOAc–hexane, 4:1) R_f 0.33. IR ν_{max}^{neat} cm^{-1}: 3375, 1597, 1507, 1487, ^{1}H NMR ($CDCl_3$, 300 MHz): δ1.78 (*tt*, *J* = 6.5, 7 Hz, H-8′), 2.57 (*t*, *J* = 7 Hz, H-7′), 2.85 (*dd*, *J* = 7, 11 Hz, H-7), 2.96 (*dd*, *J* = 7, 11 Hz, H-7), 3.42 (*dddd*, *J* = 7,7,7,7 Hz, H-8), 3.57 (*t*, *J* = 6.5 Hz, H-9′), 3.75 (*dd*, *J* = 7, 11 Hz, H-9), 3.76 (*s*, OMe), 3.83 (*s*, OMe), 3.85 (*dd*, *J* = 7, 11 Hz, H-9), 6.51 (*d*, *J* = 2 Hz, H-2′), 6.56 (*d*, *J* = 2 Hz, H-6′), 6.60 (*d*, *J* = 2 Hz, H-2), 6.61 (*dd*, *J* = 2, 8 Hz, H-6), 6.73 (*d*, *J* = 8 Hz, H-5). ^{13}C NMR ($CDCl_3$, 75 MHz): δ31.9 (C-8′), 34.4 (C-7′), 36.6 (C-7), 44.3 (C-8), 55.8 (OMe), 55.9 (OMe), 62.1 (C-9′), 65.2 (C-9), 109.2 (C-6′), 111.7 (C-2), 114.0 (C-2′), 120.7 (C-6), 121.7 (C-5), 127.3 (C-3′), 132.3 (C-1), 133.0 (C-1′), 141.8 (C-4′), 143.6 (C-4), 146.2 (C-3), 146.5 (C-5′). EIMS (70 eV) *m/z* (rel. int.) 362 $[M]^+$ (20), 224 (5), 208 (67), 179 (25), 164 (15), 151 (12), 137 (100). HRMS for $C_{20}H_{26}O_6$ requires 362.1730; found $[M]^+$ *m/z* 362.1731.

Treatment of **17a** (18 mg) with Ac_2O (0.5 ml) in pyridine (0.5 ml) for 16 hr gave the corresponding tetraacetate **17** (19 mg) after usual work-up.

Agatharesinol tetraacetate (**18**). Gum. $[\alpha]_D^{25}$ −20° ($CHCl_3$; *c* 1.3) [lit. [17] $[\alpha]_D^{25}$ −19° (Me_2CO; *c* 1.0)]. ^{13}C NMR ($CDCl_3$, 75 MHz): δ50.0 (C-7), 64.0 (C-9), 72.8



Scheme 1.

(C-8), 121.7 (C-3, 5, 3′, 5′), 127.3 (C-2′, 6′), 128.0 (C-8′), 129.2 (C-2, 6), 131.9 (C-7′), 134.4 (C-1′), 137.0 (C-1), 149.6 (C-4), 150.2 (C-4′), 20.7, 20.7, 21.1, 21.1, 169.3, 169.4, 170.2, 170.6 (4 × OAc).

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