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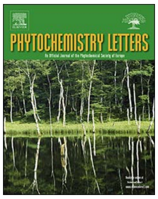

Two new sesquarterpenoids from the bark of *Cryptomeria japonica*

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ABSTRACT

Two new sesquarterpenoids, *i.e.* ferrugicadinol A (**1**) and ferrugicryptomeridiol (**3**), and one known sesquarterpenoid, ferrugicadinol (**2**) were isolated from the bark of *Cryptomeria japonica* D. Don. Their structures were identified by extensive spectral analysis and comparison with the data of known analogues.

1. Introduction

Cryptomeria japonica D. Don belongs to the family Cupressaceae and is the only species existing in the genus *Cryptomeria*. It is endemic to Japan, known as sugi (Japanese cedar) in Japanese (Gan, 1958); and has been an important plantation coniferous tree species in Taiwan since 1906. *C. japonica* is a massive evergreen coniferous tree, growing up to 50 m in height. Its wood is aromatic, soft, lightweight but sturdy, waterproof, and reddish-pink in color and has been used as a building material for Japanese-style houses and other wood products. Previous phytochemical investigations of the leaves, heartwood, and barks of *C. japonica* have resulted in the isolation of diverse terpenoids, including monoterpenoids, sesquiterpenoids, and diterpenoids (Arihara et al., 2004a, 2004b; Chen et al., 2001; Kofujita et al., 2001, 2002; Morita et al., 1995; Nagahama and Tazaki, 1993; Nagahama et al., 1993, 1996a, 1996b, 1998; Narita et al., 2006; Shibuya, 1992; Shieh et al., 1981; Shimizu et al., 1988; Su et al., 1993, 1994a, 1994b, 1995a, 1995b, 1996; Morisawa et al., 2002; Yoshikawa et al., 2006a, 2006b). Several crude extracts and secondary metabolites of this plant have been reported to exhibit antibacterial (Li et al., 2008), antifungal (Kofujita et al., 2001), cytotoxic (Kofujita et al., 2002), anti-inflammatory (Shyur et al., 2008), anti-androgenic (Tu et al., 2007), and insect antifeedant (Wu et al., 2008), and repellent (Morisawa et al., 2002) properties. As part of our studies on the new chemical ingredients of the bark of *C. japonica*, we have already reported the isolation of a cytotoxic sesquarterpene (C_{35}), cryptotrione, with an unprecedented skeleton possessing a conjugated abietane and cadinane (Chen et al., 2010) and five abietane-type diterpenoids (Chang et al., 2016). In this report, we describe the isolation and structure elucidation of two new sesquarterpenoids (Fig. 1).

2. Results and discussion

A methanol extract of the bark of *C. japonica* was suspended in H_2O and then partitioned successively with EtOAc and *n*-BuOH. The EtOAc fraction was subjected to repeated silica gel column chromatography

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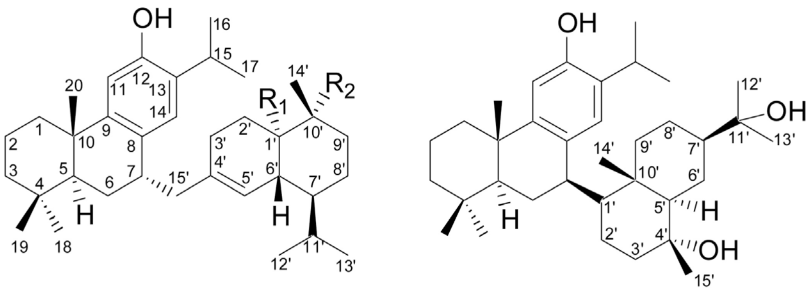

1 R_1=OH, R_2=H
2 R_1=H, R_2=OH

3

Fig. 1. Structures of compounds **1**-**3**.

and semipreparative NP-HPLC to afford two new sesquarterpenoids, ferrugicadinol A (**1**) and ferrugicryptomeridiol (**3**) and one known sesquarterpenoid, ferrugicadinol (**2**) (Hsieh et al., 2006) (Fig. 1).

Table 1
^{1}H NMR data for compounds **1** and **3**. (CDCl$_3$, δin ppm, J in Hz, 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR).

No.	**1**		**3**	
	δ_C	δ_H	δ_C	δ_H
1	38.7	1.34 m, 2.14 br d (12.5)[a]	38.7	1.36 m, 2.17 br d (12.5)
2	19.3	1.57 m, 1.72 m	19.2	1.66 m, 1.58 m
3	41.7	1.22 m, 1.47 m	42.1	1.23 m
4	33.2		34.0	
5	45.1	1.38 m	46.3	1.40, m
6	22.1	1.63 m	21.6	1.90 br d (14.4), 1.61 m
7	34.9	2.85 m	32.7	3.14 br d (8.8)
8	131.5		131.4	
9	148.8		149.8	
10	37.9		37.0	
11	110.6	6.53 s	109.9	6.61 s
12	150.7		150.6	
13	131.4		131.2	
14	127.5	6.83 s	126.7	6.99 s
15	26.9	3.09 sept (7.0)	27.1	3.10 sept (6.9)
16	22.7	1.22 d (7.0)	22.7	1.21 d (6.9)
17	22.5	1.23 d (7.0)	22.5	1.21 d (6.9)
18	33.7	0.94 s	33.2	0.97 s
19	21.6	0.88 s	21.2	0.86 s
20	24.8	1.12 s	24.2	1.03 s
1′	73.1		58.7	1.66 m
2′	27.5	1.74 m, 2.01 m	22.5	1.75 m
3′	24.0	2.17 m, 2.37 m	43.8	1.76 m, 1.30 m
4′	137.3		72.1	
5′	123.1	5.37 s	56.5	1.33 m
6′	45.2	2.39 br s	21.3	1.50 m, 1.16 m
7′	40.9	1.51 m	49.3	1.42 m
8′	23.6	1.68 m, 1.16 m	21.0	1.95 br d (12.2), 1.51 m
9′	28.7	1.56 m, 1.31 m	42.0	2.09 br d (11.2), 1.42 m
10′	39.3	1.78 m	38.4	
11′	29.3	1.55 m	73.0	
12′	21.4	0.93 d (7.0)	27.1	1.22 s
13′	21.1	0.90 d (7.0)	27.2	1.22 s
14′	15.4	1.08 d (7.0)	16.2	0.99 s
15′	47.7	2.26 t (15.2), 2.18 m	22.7	1.10 s

[a] Coupling constants are presented in Hz.

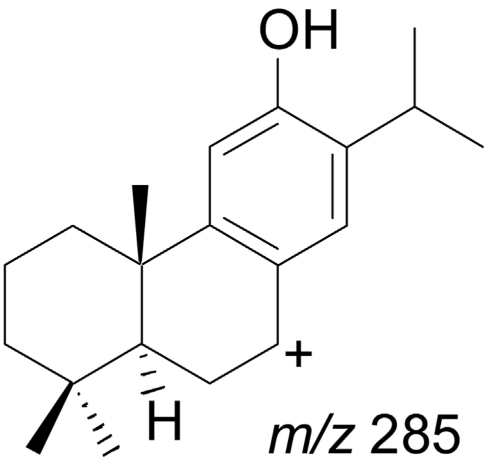

Fig. 2. EI-MS fragmental ion.

The IR spectrum of **1** indicated the presence of the aromatic (1610 and 1507 cm^{-1}) and hydroxy (3409 cm^{-1}) groups. Its HR-EI-MS gave a molecular ion at m/z 506.8120, establishing the molecular formula of **1** as $C_{35}H_{54}O_2$, with nine degrees of unsaturation. The base peak of EI-MS fragmental ions of **1** at m/z 285 [$C_{20}H_{29}O$]$^+$ (Fig. 2) indicated that **1** should be a dimer of diterpene and sesquiterpene. The ^{1}H and ^{13}C NMR data of **1** (Table 1) were similar to those of the known compound, sugikurojin H with a abietane incorporate cadinane skeleton, isolated from the bark of *C. japonica* (Yoshikawa et al., 2006b). One set of dehydroabietane proton signals including three tertiary-linked methyls [δ_H 0.88, 0.94, 1.12 (3H each, s, Me-19, Me-18, Me-20)], an isopropyl group attached on the benzene ring [δ_H 1.22 (3H, d, J = 7.0 Hz, Me-16), 1.23 (3H, d, J = 7.0 Hz, Me-17), 3.09 (1H, sept, J = 7.0 Hz, H-15)], two singlet phenyl protons [δ_H 6.53 (1H, s, H-11), 6.83 (1H, s, H-14)], and a typical downshifted H$_\beta$-1 signal [δ_H 2.14 (1H, br d, J = 12.5 Hz)] of dehydroabietane (Yoshikawa et al., 2006b) was observed in the ^{1}H NMR spectrum of **1**. The ^{1}H and ^{13}C NMR data of diterpene moiety of **1** (Table 1) closely resembled those of ferruginol (Tezuka et al., 1998) and sugikurojin H (Yoshikawa et al., 2006b), which led to establish the partial structure of **1** as a ferruginol with a substituent at C-7. The relative configurations of sterogenic C-atoms in ferruginol were determined by significant NOE correlations between H-5 (δ_H 1.38)/H-15′ (δ_H 2.26) and Me-19 (δ_H 0.88)/Me-20 (δ_H 1.12) in the nuclear Overhauser enhancement exchange spectroscopy (NOESY) spectrum (Fig. 3). With the aid of ^{1}H–^{1}H COSY, the ^{1}H NMR spectrum of **1** (Table 1) also revealed one set of sesquiterpene signals as follows: one isopropyl group [δ_H 0.90 (3H, d, J = 7.0 Hz, Me-13′), δ_H 0.93 (3H, d, J = 7.0 Hz, Me-12′), and 1.55 (1H, m)], one doublet methyl [δ_H 1.08 (3H, d, J = 7.0 Hz, Me-14′)], one downshifted methine [δ_H 2.39 (1H, br s, H-6′)], and one olefinic proton [5.37 (s, H-5′)]. Additionally, six of a total of nine degrees of unsaturation was accounted for ferruginol and one was attributable to a double bond, the remaining two degrees of unsaturation hinted that **1** exhibited a bicyclic sesquiterpene moiety. By comparison of ^{13}C NMR data of **1** (Table 1) with cadinane sesquiterpenes, 1-methoxy-4-cadinene (Arihara et al., 2004b) and cubenol (Oyarzun and Garbarino, 1988), the sesquiterpene moiety of **1** was tentatively proposed to be an α-cadinenol derivative. The NOE correlations between H-6′ (δ_H 2.39)/Me-12′ (δ_H 0.93) and Me-14′ (δ_H 1.08), HMBC correlations between Me-14′/C-1′ (δ_C 73.1) and C-9′ (δ_C 28.7) (Fig. 3), together with the broad singlet of the olefinic proton (H-5′) (Kuo et al., 2003; He et al., 1997), indicated that α-cadinol derivative exhibited a *trans* ring junction and a hydroxy group located on C-1′ in