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18-OXOFERRUGINOL FROM THE LEAF OF *TORREYA NUCIFERA*

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Key Word Index—*Torreya nucifera*; Taxaceae; diterpenoids; abietanes; 18-oxoferruginol.

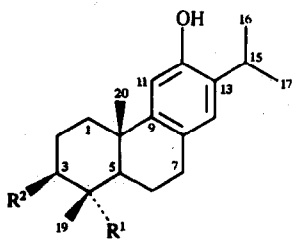
Abstract—From the leaf of the conifer *Torreya nucifera*, a new diterpenoid has been isolated and shown to be 18-oxoferruginol (12-hydroxy-8,11,13-abietatrien-18-al) on the basis of its spectroscopic properties and its chemical conversion to the known 18-hydroxyferruginol (8,11,13-abietatriene-12,18-diol).

INTRODUCTION

The Japanese nutmeg *Torreya nucifera* Sieb. et Zucc. (Taxaceae) has been reported to contain a number of sesquiterpenoids [1] and labdane [2] and abietane [3] diterpenoids. A further investigation of the constituents of the leaf of *T. nucifera* has afforded the known compounds ferruginol (**1**), 18-hydroxyferruginol (**2**), communic acid, isopimaric acid, kayadiol, hinokiol (**3**), (2*E*,6*E*)-farnesol and δ-tocopherol. In addition, a novel crystalline diterpenoid, 18-oxoferruginol (12-hydroxy-8,11,13-abietatrien-18-al) (**4**), was obtained.

RESULTS AND DISCUSSION

18-Oxoferruginol, $C_{20}H_{28}O_2$ (*m/z* 300.2108), from the leaf of *T. nucifera* collected in Tokushima Prefecture, Japan has mp 139–141° and $[\alpha]_D$ + 69.6. The IR spectrum showed bands at 3600 and 1723 cm^{-1}, associated with a hydroxyl group and an aldehyde, respectively, whilst the UV spectrum (λ_{max} 284 nm) indicated the presence of a phenol. The ^1H NMR spectrum revealed the presence of an aldehyde group [δ9.26 (*s*, H-18)], two aromatic protons [δ6.84 (*s*, H-14) and 6.64 (*s*, H-11)], a hydroxyl proton [δ5.37 (*br s*, OH)], an isopropyl group [δ3.13 (*septet*, J = 6.8 Hz, H-15), 1.23 and 1.22 (both *d*, J = 6.8 Hz, 3H-16 and 3H-17)], a benzylic methylene [δ2.81 (*m*, 2H-7)], and two tertiary methyl groups [δ1.21 and 1.15 (both *s*, 3H-19 and 3H-20)]. Consideration of these data suggested an abietane or sempervirane skeleton in which ring C is aromatized and bears a hydroxyl substituent. The latter possibility was discounted following difference NOE experiments. Thus, irradiation of the lower field aromatic proton enhanced the resonance of the isopropyl methine proton (3.5%) as well as that of the benzylic methylene (7.5%). Irradiation of the other aromatic signal increased both the phenolic hydroxyl resonance (11.0%) and a signal at δ2.20 (*br d*, J = 13.1 Hz) (13.1%). The latter resonance must be due to H-1β which is deshielded due to it being in the plane of the aromatic ring. The position of the carbonyl group was shown to be C-18 by comparison of the ^{13}C NMR spectrum (see Table 1) with those of other aromatic diterpenoids [4]. The absence of a methyl resonance at *ca* 33 ppm indicated that either C-18 or C-19 had been oxidized. The upfield shift of a methyl signal to 14.04 ppm established the position of oxygenation as C-18, since the C-4 epimer would not be expected to have a high-field



1 R^1 = Me, R^2 = H
2 R^1 = CH_2OH, R^2 = H
3 R^1 = CH_2OH, R^2 = OH
4 R^1 = CHO, R^2 = H

Table 1. ^{13}C chemical shifts for diterpenoids (**1–4**)

Carbon	1	2	3*	4
1	38.84 *t*	38.48 *t*	36.81 *t*	37.81 *t*
2	19.24 *t*	18.64 *t*	27.52 *t*	17.75 *t*
3	41.70 *t*	35.10 *t*	78.44 *d*	32.01 *t*
4	33.42 *s*	37.31† *s*	38.79 *s*	49.83 *s*
5	50.35 *d*	43.89 *d*	49.76 *d*	42.79 *d*
6	19.31 *t*	19.00 *t*	18.93 *t*	21.51 *t*
7	29.75 *t*	29.35 *t*	29.88 *t*	28.98 *t*
8	127.23 *s*	127.01 *s*	125.92 *s*	126.56 *s*
9	148.62 *s*	148.28 *s*	147.33 *s*	147.11 *s*
10	37.50 *s*	37.85† *s*	37.10 *s*	36.23 *s*
11	110.98 *d*	110.96 *d*	110.60 *d*	110.81 *d*
12	150.66 *s*	150.76 *s*	151.46 *s*	150.91 *s*
13	131.43 *s*	131.60 *s*	132.18 *s*	132.09 *s*
14	126.59 *d*	126.60 *d*	126.16 *d*	126.81 *d*
15	26.79 *d*	26.82 *d*	26.36 *d*	26.79 *d*
16	22.57† *q*	22.55† *q*	22.38† *q*	22.51† *q*
17	22.76† *q*	22.74† *q*	22.55† *q*	22.76† *q*
18	33.30 *q*	72.23 *t*	27.90 *q*	206.46 *d*
19	21.62 *q*	17.40 *q*	15.19 *q*	14.04 *q*
20	24.78 *q*	25.15 *q*	24.57 *q*	24.94 *q*

Measured at 100.5 MHz in $CDCl_3$ (* in $CDCl_3$ + CD_3OD). Shifts in δ relative to $CDCl_3$ at δ77.00. Multiplicities were determined using the INEPT pulse sequence.

†Values may be interchanged within a column.

methyl resonance in its ^{13}C NMR spectrum. Thus, the structure of the hydroxy aldehyde must be 18-oxoferruginol (12-hydroxyabieta-8,11,13-trien-18-al) (**4**). Reduction of the aldehyde group with $LiAlH_4$ in Et_2O afforded a crystalline diol, identical to 18-hydroxyferruginol (**2**) [3], and thus established **4** as belonging to the normal series of absolute configuration. Additionally, the ^{13}C NMR spectra of 18-hydroxyferruginol (**2**) and hinokiol (**3**) were measured for the first time. The assignments are shown in Table 1.

EXPERIMENTAL

Mps are uncorr. IR and UV spectra were recorded in CCl_4 and EtOH, respectively. NMR spectra were recorded for $CDCl_3$ solutions (^1H, 400 MHz; ^{13}C, 100.5 MHz). Chemical shifts were measured relative to TMS (δ0.00, ^1H) or $CDCl_3$ (δ77.00, ^{13}C).

Torreya nucifera was collected in Tokushima Prefecture, Japan in October, 1985. The leaves (11 kg) were removed and ground. Extraction with MeOH (40 l., × 2) afforded a crude extract (243 g) which was macerated with cold Et_2O (1 l. × 2). The Et_2O soluble material (167 g) was subjected to CC (silica gel) using an EtOAc–hexane gradient. Further fractionation of the extract by CC and gel permeation chromatography (Sephadex LH-20 MeOH–$CHCl_3$ 1:1 as eluant) afforded, in order of elution, ferruginol (650 mg), (2*E*,6*E*)-farnesol (17 mg), δ-tocopherol (20 mg), 18-oxoferruginol (1.5 g), 18-hydroxyferruginol (5.8 g), communic acid (1.4 g), isopimaric acid (650 mg), kayadiol (125 mg), and hinokiol (355 mg). Known compounds were identified by comparison of their spectroscopic properties with literature values.

18-Oxoferruginol (**4**) was recrystallized from hexane, mp 139–141°, $[\alpha]_D$ +69.6 (*c*, 1.05 in $CHCl_3$), ν_{max} 3600, 2950, 1723, 1620, 1499, 1412, 1379, 1360, 1321, 1307 and 914 cm^{-1}, λ_{max} nm (log ε) 284 (3.5) ^1H NMR: see Results and Discussion. ^{13}C NMR: see Table 1. EIMS 70 eV *m/z* (rel. int.): 300.2108 ($C_{20}H_{28}O_2$ requires *m/z* 300.2092) $[M]^+$ (100), 285 (39.1), 267 (12.2), 257 (22.2), 243 (14.9), 225 (12.4), 201 (16.8), 189 (27.0), 175 (19.2), 147 (16.1), 43 (11.2).

Reduction of 18-oxoferruginol. To a stirred ice-cold soln of $LiAlH_4$ (100 mg) in dry Et_2O (10 ml) was added 18-oxoferruginol (50 mg) in dry Et_2O (1 ml). After 30 min the reaction mixture was quenched by the careful addition of wet Et_2O. 10% aq. HCl (25 ml) was added and the mixture extracted with Et_2O (25 ml × 2). The combined organic layers were washed with aq. $NaHCO_3$ (25 ml) and dried over anhydrous $MgSO_4$. Removal of solvent afforded 18-hydroxyferruginol (47 mg), identical in all respects to the natural product from *T. nucifera* [3].

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