Pergamon

Tetrahedron Letters 40 (1999) 6419–6422

TETRAHEDRON LETTERS

Standishinal, a novel carbon skeletal diterpene from the bark of *Thuja standishii* (Gord.) Carr.

Hironori Ohtsu, Manabu Iwamoto, Hirofumi Ohishi, Shunyo Matsunaga and Reiko Tanaka *

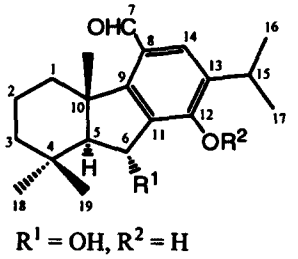
Department of Medicinal Chemistry, Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan

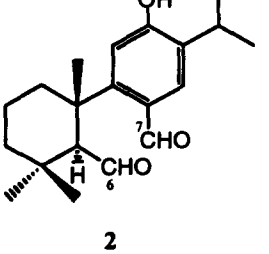
Received 19 April 1999; revised 7 June 1999; accepted 11 June 1999

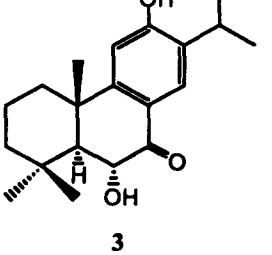
Abstract

Standishinal (**1**), a new irregular abietane-type diterpenoid, was isolated from the bark of *Thuja standishii* and the absolute stereostructure was established by 2D NMR and X-ray crystallographic analyses. It was found that treatment of 12-hydroxy-6,7-*seco*-abieta-8,11,13-triene-6,7-dial (**2**) with $BF_3 \cdot OEt_2$ at 0°C in CH_2Cl_2 furnished compound **1**.

The $CHCl_3$ extract (560 g) of the fresh stem bark (2.6 kg) of *Thuja standishii* (Cupressaceae) was carefully chromatographed on a silica gel, Sephadex LH-20, and medium-pressure liquid chromatography column (ODS) to give a novel skeletal diterpenoid, standishinal (**1**, 78 mg) and two known compounds, 12-hydroxy-6,7-*seco*-abieta-8,11,13-triene-6,7-dial (**2**, 34 mg),[1] and 6α-hydroxysugiol (**3**, 3 mg).[2] In this communication, we report the absolute stereostructure of **1** and its biomimetic synthesis from **2**.







1 $R^1 = OH$, $R^2 = H$ **2** **3**

1a $R^1 = OAc$, $R^2 = Ac$

1b $R^1 = H$, $\Delta^{5(6)}$, $R^2 = p\text{-}BrC_6H_4CO$

Standishinal (**1**)[3] has the molecular formula $C_{20}H_{28}O_3$ (*m/z* 316.2021) deduced by the high-resolution MS spectrum. The UV and IR spectra showed the presence of a hydroxyl group (ν_{max} 3327 cm^{-1}), a conjugated aldehyde group [λ_{max} 288 nm (log ε 4.1); ν_{max} 1662 cm^{-1}] and a benzene ring (ν_{max} 1609, 1578 cm^{-1}). The DEPT spectrum showed five methyl groups, three methylene groups, two methine

* Corresponding author.

0040-4039/99/$ - see front matter
PII: S0040-4039(99)01191-0

groups, two quaternary carbons, a hydroxy methine group, an aldehyde carbon, an sp^2 methine and five sp^2 quaternary carbon atoms. The ^1H and ^{13}C NMR spectra (Table 1) showed three tertiary methyl groups (δ_H 1.17, 1.19 and 1.25), an isopropyl group attached to a benzene ring [δ_H 1.24, 1.25 (each d, J=7.0 Hz) and 3.27 (1H, septet, J=7.0 Hz)], a secondary hydroxyl group [δ_H 5.40 (1H, d, J=10.0 Hz); δ_C 75.5 (d)], and a pentasubstituted benzene ring [δ_H 7.69 (1H, s)]. The presence of a phenolic hydroxyl group was proved by the fact that acetylation of **1** afforded a diacetate (**1a**)[4] [δ_H 2.12 and 2.27 (each 3H, s)]. The HMBC spectrum (Fig. 1) indicated the long-range correlations between H-6 and C-5, C-11 and C-12, and between H-7 and C-8, C-9 and C-14. Furthermore, in the ^1H–^1H COSY spectrum (Fig. 1), H-6 was correlated with only H-5. Therefore, **1** has a novel 6(7→11)*abeo*-abietane skeleton bearing two hydroxyl groups attached at C-6 and C-12, and a formyl group at C-8. The relative stereochemistry of **1** was defined by a NOESY experiment (Table 1). Significant NOEs were observed between: (i) H-6β and H-19 and H-20; and (ii) H-7 and H-14 and H-20. Thus, the relative stereostructure of **1** was proved as depicted. In order to determine the absolute stereostructure of **1**, we conducted the X-ray crystallographic analyses of **1**[5] and 1-*p*-bromobenzoate (**1b**)[6] in which the C-6 hydroxyl group was dehydrated. The absolute configuration of **1b** was determined using anomalous scattering factors of the bromine atom and the Bijovet reflection data. Fig. 2 shows the ORTEP view of **1** and **1b**, and the absolute stereostructure was established as shown in **1**. Standishinal (**1**) possessing a novel carbon skeleton, 8-formyl-6(7→11)*abeo*-abietane, is the first example in nature.

Table 1
^1H and ^{13}C NMR data for **1** (in $CDCl_3$)[a]

Position	^1H (500 MHz, J in Hz)	^{13}C (125 MHz)	NOESY
1α	1.76 ddd (12.0, 12.0, 4.0)	38.4 (t)	1β, 2α
β	2.46 dt (12.0, 3.0)		1α, 2α, 2β, 7, 20
2α	1.70 m	19.9 (t)	1α, 1β, 2β, 3β
β	1.88 m		1β, 2α, 3β, 19, 20
3α	1.25 m	41.0 (t)	1α, 5α, 18
β	1.53 dt (13.5, 3.5)		2α, 2β
4	-	33.4 (s)	
5α	1.83 d (10.0)	67.2 (d)	18
6β	5.40 d (10.0)	75.5 (d)	19, 20
7	10.21 s	189.9 (d)	1β, 14, 20
8	-	153.9 (s)	
9	-	124.5 (s)	
10	-	46.8 (s)	
11	-	127.2 (s)	
12	-	157.3 (s)	
13	-	134.5 (s)	
14	7.69 s	128.5 (d)	7, 16, 17
15	3.27 septet (7.0)	26.5 (d)	16, 17
16	1.24 d (7.0)[b]	22.3 (q)[c]	14, 15, 17
17	1.25 d (7.0)[b]	22.4 (q)[c]	14, 15, 16
18	1.17 s	22.0 (q)	3α, 5α
19	1.19 s	34.0 (q)	2β, 6β, 20
20	1.26 s	23.9 (q)	2β, 6β, 7, 19

[a] Assignments were made by ^1H-^1H COSY, HMQC, HMBC and NOESY data.
[b, c] Assignments in each column may be interchanged.

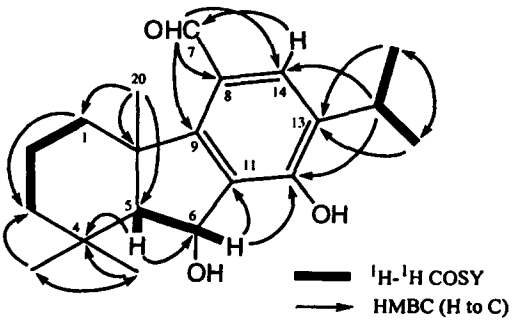
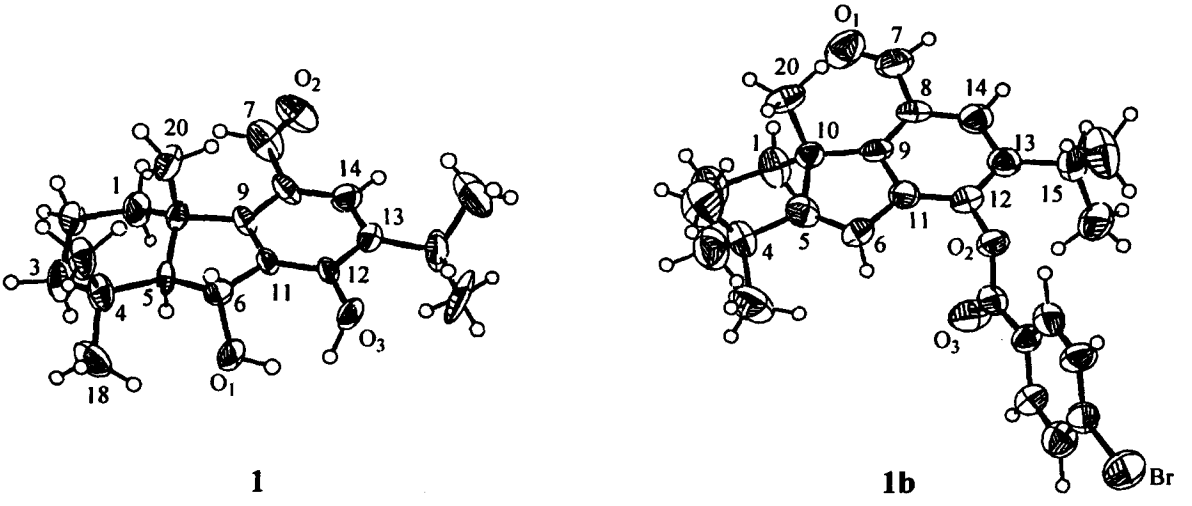


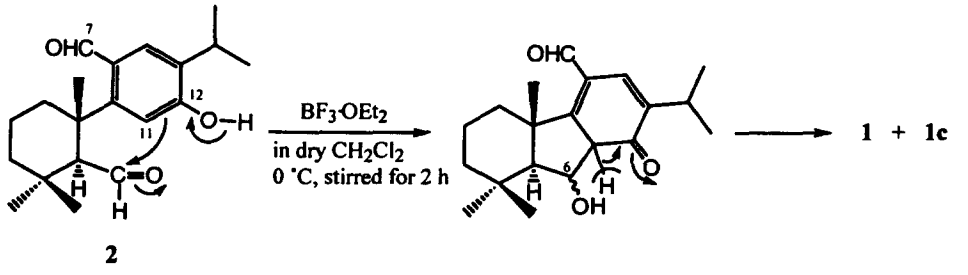
Figure 1. ^{1}H–^{1}H COSY and HMBC correlations of **1**



1 **1b**

Figure 2. ORTEP drawing of **1** and **1b**

From the biogenetical viewpoint, **1** was considered to be biosynthesized from **2** by attack of the C-11 double bond on the C-6 aldehyde group. An attempt to convert compound **2** to compound **1** was successful (Scheme 1). Treatment of **2** (5 mg) with $BF_3 \cdot OEt_2$ (20 μl) in dry CH_2Cl_2 at 0°C for 2 h afforded **1** (1.2 mg, $[\alpha]_D^{23}$ −73.6 (*c* 0.25, $CHCl_3$)) and the 6β-epimer of **1** (**1c**, 0.7 mg).[7] The former product was identical with natural compound **1**. This chemical correlation confirmed the possible biosynthetic pathway of **1** from **2** in the plant organ.



2

Scheme 1.

Acknowledgements

The authors are grateful to Mr. Katsuhiko Minoura and Mrs. Mihoyo Fujitake of this University for NMR and MS measurements.

References

1. Fang, J.-M.; Jan, S.-T.; Cheng, Y.-S. *J. Chem. Res. (S)* **1986**, 350.
2. Su, W.-C.; Fang, J.-M.; Cheng, Y.-S. *Phytochemistry* **1994**, *35*, 1279.
3. Compound **1**: colorless needles, mp 164–165.5°C (*n*-hex-$CHCl_3$), $[\alpha]_D^{25}$ –90.7 (*c* 0.56, $CHCl_3$); HREIMS *m/z* 316.2021 $[M]^+$ (calcd. $C_{20}H_{28}O_3$: 316.2037); UV λ_{max} (EtOH): 288 nm (log ε 4.1); IR (film) ν_{max} cm^{-1}: 3327 (OH), 1662 (Ph–CHO), 1609, 1578 (benzene ring), 1261 (Ph–C–O–); EIMS *m/z* (rel. int.): 316 $[M]^+$ (32), 298 (92), 255 (31), 242 (27), 229 (83).
4. Compound **1a**: colorless needles, mp 136–137°C (*n*-hex-EtOAc), $[\alpha]_D^{23}$ +19.1 (*c* 0.33, $CHCl_3$); IR (film) ν_{max} cm^{-1}: 1770 (Ph–OAc), 1738 (OAc), 1688 (Ph–CHO), 1609, 1574 (benzene ring); EIMS *m/z* (rel. int.): 340 $[M–HOAc]^+$ (8), 298 (100), 283 (76), 229 (85), 199 (19), 43 (13); ^1H NMR ($CDCl_3$): δ 0.94 (3H, s, H-19), 1.14 (3H, s, H-18), 1.20 and 1.22 (each 3H, d, *J*=7.0 Hz, H-16 and H-17), 1.26 (1H, m, H-3α), 1.30 (3H, s, H-20), 1.51 (1H, dt, *J*=13.5, 3.0 Hz, H-3β), 1.72 (1H, m, H-2α), 1.88 (2H, m, H-1α and H-2β), 2.08 (1H, d, *J*=10.0 Hz, H-5α), 2.12 and 2.27 (each 3H, s, -OCO*Me*×2), 2.45 (1H, dt, *J*=12.0, 3.0 Hz, H-1β), 2.92 (1H, septet, *J*=7.0 Hz, H-15), 6.52 (1H, d, *J*=10.0 Hz, H-6β), 7.82 (1H, s, H-14), 10.42 (1H, s, H-7); ^{13}C NMR ($CDCl_3$): δ 19.9 (t, C-2), 20.8 and 21.5 (each q, -OCO*Me*×2), 22.0 (q, C-18), 22.7 and 23.2 (each q, C-16 and C-17), 25.4 (q, C-20), 27.1 (d, C-15), 32.7 (q, C-19), 33.2 (s, C-4), 38.8 (t, C-1), 40.9 (t, C-3), 46.9 (s, C-10), 63.2 (d, C-5), 73.2 (d, C-6), 127.8 (d, C-14), 128.5 (s, C-9), 129.9 (s, C-11), 140.3 (s, C-13), 149.6 (s, C-8), 155.0 (s, C-12), 168.3 and 170.7 (each s, -O*C*OMe×2), 190.1 (d, C-7).
5. The crystal data for **1** are as follows: data were acquired with a Rigaku AFC5R diffractometer, Cu-Kα radiation (λ=1.54178 Å), graphite monochromated, orthorhombic, $C_{20}H_{28}O_3$ (MW: 316.441), space group $P2_12_12_1$ with *a*=9.684 (3), *b*=23.019 (11), *c*=8.073 (3) Å, *V*=1799 (1) $Å^3$, *Z*=4, and $D_{(calc)}$=1.1680 g cm^{-1}. The final *R* value was 0.128 for 1117 reflections. The supplementary materials have been deposited at the Cambridge Crystallographic Data Centre.
6. The crystal data for **1b** are as follows: orthorhombic, $C_{27}H_{29}O_3Br$ (MW: 481.430), space group $P2_12_12_1$ with *a*=14.132 (3), *b*=25.144 (9), *c*=6.660 (3) Å, *V*=2366 (1) $Å^3$, *Z*=4, and $D_{(calc)}$=1.3513 g cm^{-1}. The final *R* value was 0.0825 for 2311 reflections. The supplementary materials have been deposited at the Cambridge Crystallographic Data Centre.
7. Compound **1c**: IR (film) ν_{max} cm^{-1}: 3360 (OH), 1665 (Ph–CHO), 1607, 1562 (benzene ring); EIMS *m/z* (rel. int.): 298 $[M–H_2O]^+$ (56), 283 $[M–H_2O–Me]^+$ (42), 255 (9), 242 (13), 229 (100); ^1H NMR ($CDCl_3$): δ 1.25 (3H×2, s, H-18 and H-19), 1.28 (3H, s, H-20), 1.30 and 1.32 (each 3H, d, *J*=7.0 Hz, H-16 and H-17), 3.20 (1H, septet, *J*=7.0 Hz, H-15), 5.25 (1H, br s, H-6α), 7.55 (1H, s, H-14), 10.24 (1H, s, H-7).