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Taxodal, a novel irregular abietane-type diterpene from the cones of *Taxodium distichum*

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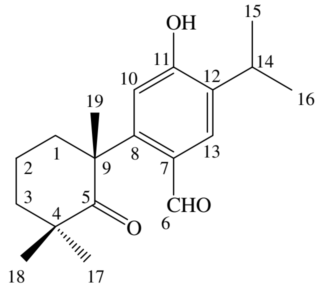
ABSTRACT

One novel irregular abietane-type diterpene denominated taxodal **1** was isolated from the cones of *Taxodium distichum*. The structure was estimated on the basis of NMR spectral data and confirmed by X-ray crystallographic analysis.

Taxodium distichum Rich. (Taxodiaceae) is an extant deciduous fossil conifer derived from Mexico and it is known that the abietane-type diterpenoids are the major compounds in cones of *Taxodium* species by the previous studies on fossil conifer and sediments of ancient flora.[1–3] It has been reported that the several kinds of abietane-type diterpenes, such as taxodione and taxodone, were isolated from the cone of *T. distichum*.[4,5]

Recently, taxodistine A and B, novel terpenoids, were isolated from the cone and reported to show cytotoxic activity[6] same as taxodione and taxodone.[7] In the study of self-defense bioactivity, we have investigated the cone of *T. distichum* and reported the isolation and stereo-structural elucidation of taxodal **1** (Fig. 1), a characteristic new decarbonized abietane-type diterpene, which was isolated together with several known abietane-type diterpenes. To determine the stereo-structural elucidation of irregular abietane-type diterpene **1** is valuable for deliberate biosynthesis for novel learning of abietane-type diterpenes derived from natural compounds.

Air-dried fallen cones of *T. distichum* (800 g) were extracted with *n*-hexane. The *n*-hexane soluble fraction (88.6 g) was extracted by partition extraction with saturated $NaHCO_3$, 10% $NaCO_3$ and 1% NaOH aqueous solution in a separatory funnel to yield 1.4 g, 1.2 g and 11.2 g fractions, respectively, along with 74.76 g residue fraction. Taxodal **1** (44.6 mg), a characteristic compound was isolated from fraction of 1% NaOH aqueous solution after silica gel 60 N column chromatography (hexane/EtOAc = 20:1).



1

Figure 1. Structure of taxodal **1**.

Taxodal **1** which named 4-hydroxy-5-isopropyl-2-(1,3,3-trimethyl-2-oxocyclohexyl)benzaldehyde according to the IUPAC nomenclature, was precipitated as white transparent needles in hexane–benzene; mp 233–234 °C; $[\alpha]_D$ 131.4 (*c* 0.005 g/ml, 20 °C, MeOH); UV λ_{max} (EtOAc): 285.5 nm (1.97). The molecular formula of **1** was determined to be $C_{19}H_{26}O_3$ on the basis of ^{13}C NMR and EI-MS [m/z 302.25 (M+, 26%), 287 (3), 274 (8), 269 (2), 259 (9), 256 (3), 241 (5), 232 (9), 231 (51), 220 (55), 219 (36), 205 (14), 204 (18), 203 (100), 191 (29), 190 (22), 189 (15), 187 (16), 177 (17),

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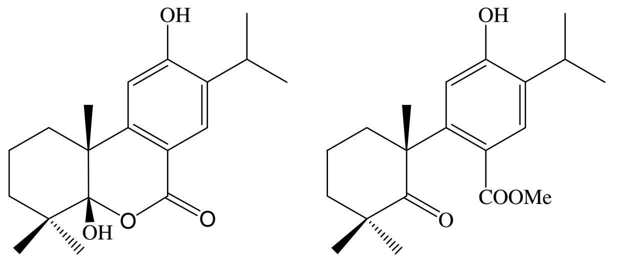
175 (16), 161 (22), 159 (10), 147 (12), 128 (14), 115 (15), 91 (16), 77 (11), 69 (11), 55 (27)] data. The IR spectrum of **1** showed absorption bands at $\gamma_{\max}$ 3230 cm^{-1} for hydroxyl group, 1689 cm^{-1} and 1666 cm^{-1} for ketone structures, 1614 cm^{-1} and 1581 cm^{-1} for aromatic groups. The ^{1}H NMR spectrum (Table 1) identified two aromatic protons at δ 7.16 (1H, s, H-10) and δ 7.73 (1H, s, H-13). In addition, it showed the existence of aldehyde associated with benzene ring at δ 9.68 (1H, s,H-6) and isopropyl group at δ 3.31 (1H, sept, J = 7.0 Hz, H-14), 1.27 (3H, d, J = 7.0 Hz, H-15) and 1.26 (3H, d, J = 7.0 Hz, H-16). The ^{13}C NMR spectrum (Table 1) showed peculiar down-field signals of a ketone structure at δ 213.2 (C) and aldehyde group at δ 190.2 (CH). The ^{13}C NMR spectrum also showed six olefinic carbons at δ 158.7 (C), 146.9 (C), 136.5 (CH), 131.4 (C), 124.8 (C) and 114.3 (CH), suggesting that **1** contains one benzene ring.

Methyl(*R*)-2-(1,3,3-trimethyl-2-oxocyclohexyl)-4-hydroxyl -5-isopropylbenzoate **3**, derived by methylation of cupresol **2** (5β-hydroxy-6-oxasugiol)[8] which has similar structure to **1** isolated from the stem bark of *Cupressus goveniana* (Cupressaceae), showed similar ^{1}H NMR spectrum data to **1**, but as shown in Figure 2 this compound has a methoxy-carbonyl group instead of the formyl group showed in Figure 1. However, cupresol **2** and the derivative **3** were determined to be C-19 methyl group mentioned above that constitutes *R*-configuration,[9] so that the ORTEP view of **1** (Fig. 3) based upon X-ray crystallographic analysis[10] revealed the identical conformation of C-19 methyl group to be that of the general abietane-type diterpenes.

Table 1
NMR data for taxodal **1** (acetone-d_6, δ in ppm)

C#	δ_C[a], mult[c]	δ_H[b], mult (J in Hz)	HMBC (^{1}H–^{13}C)
1	38.9, CH_2	2.17, ddd (12.9, 13.0, 3.5) 1.62, m	
2	17.6, CH_2	1.67, m 2.04, m	
3	36.9, CH_2	2.43, ddd (13.3, 13.3, 4.0) 1.64, m	
4	43.1, C	—	
5	213.2, C	—	
6	190.2, CH	9.68, s	C-7, C-8, C-13
7	124.8, C	—	
8	146.9, C	—	
9	51.4, C	—	
10	114.3, CH	7.16, s	C-7, C-9, C-11, C-12
11	158.7, C	—	
12	131.4, C	—	
13	136.5, CH	7.73, s	C-6, C-8, C-11, C-14
14	25.5, CH	3.31, sept (7.0)	C-15, C-16
15	20.8, CH_3	1.27, d (7.0)	C-12, C-14, C-16
16	20.8, CH_3	1.26, d (7.0)	C-12, C-14, C-15
17	25.6, CH_3	1.17, s	C-3, C-4, C-5, C-18
18	28.4, CH_3	1.22, s	C-3, C-4, C-5, C-17
19	24.0, CH_3	1.55, s	C-1, C-5, C-8, C-9, C-10

[a] Spectra were recorded at 100 MHz.
[b] Spectra were recorded at 400 MHz.
[c] ^{13}C NMR multiplicities were obtained from DEPT−90 and −135.



2 3

Figure 2. Structure of cupresol **2** and the derivative **3**.

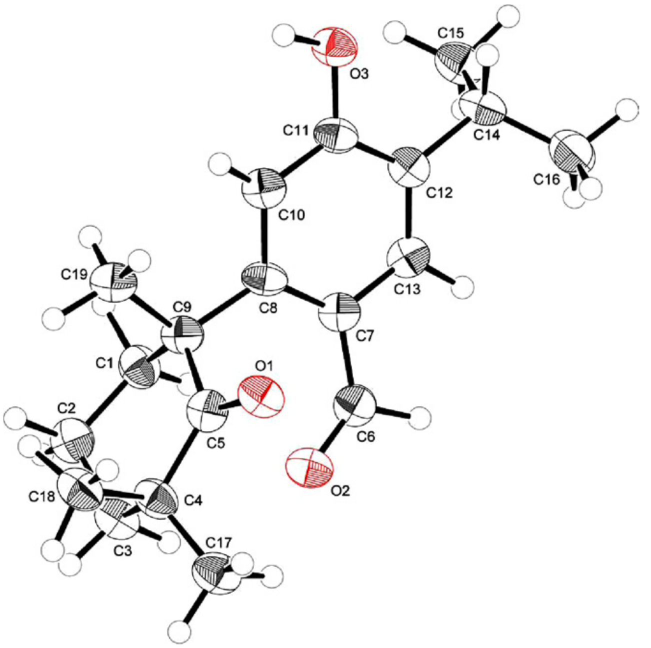


Figure 3. ORTEP view of taxodal **1**.

The total structure of **1** was determined by analysis of the 1D and 2D NMR data, including heteronuclear multiple bond connectivity (HMBC) and X-ray crystallographic analysis. The HMBC spectrum (Table 1) of **1** showed long-range couplings from H-6 to C-7, C-8 and C-13, and H-13 signal correlated to C-6, C-8, C-11 and C-14, establishing the connectivity between the benzene ring and aldehyde group. In addition, H-10 signal correlated to C-7, C-9, C-11 and C-12; H3-19 signal correlated to C-1, C-5, C-8, C-9 and C-10; and aforementioned H-13 signal correlated to C-6, C-8, C-11 and C-14, revealed the connectivity among the trimethyl-oxocyclohexyl ring, benzene ring and, isopropyl group. The final structure of **1** (Fig. 3) was revealed by NMR spectral data and X-ray crystallographic analysis, as shown in **1**.

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10. X-ray crystal data for **1** were obtained with a Rigaku RAXIS RAPID diffractometer, Mo-Kα radiation ($\lambda = 0.71075$ Å), graphite monochromator, $C_{19}H_{26}O_3$, F.W. = 302.41, orthorhombic, space group $P2_12_12_1$ (#19), cell dimensions $a = 6.810(4)$, $b = 11.268(6)$, $c = 21.796(10)$ Å, $V = 1672.5(15)$ Å^3, $Z = 4$, $D_{calc} = 1.201$ g/cm^3, μ(MoKα) = 0.793 cm^{-1}, 16405 reflections collected, 3815 unique reflections ($R_{int} = 0.151$), final R indices ($I > 2.0\sigma(I)$): $R_1 = 0.0464$, w$R_2 = 0.1243$ for 304 variable parameters. Crystallographic data for 1 have been deposited in the Cambridge Crystallographic Data Centre with the deposition numbers of CCDC 685499. Copies of these data can be obtained free of charge via www.ccdc.ca-m.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB21EZ, UK; Fax: +44 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk).