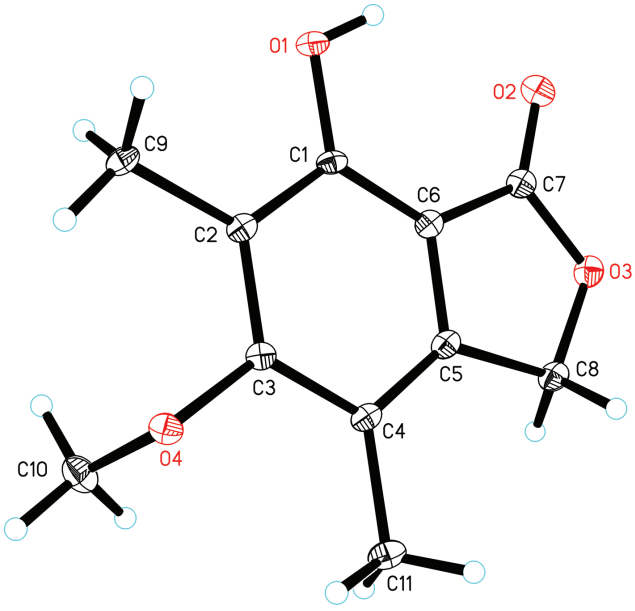
Pei-Wen Chen and Yi-Wen Tao*

Crystal structure of 7-hydroxy-5-methoxy-4,6-dimethylisobenzofuran-1(3*H*)-one, $C_{11}H_{12}O_4$



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Abstract

$C_{11}H_{12}O_4$, monoclinic, $P2_1/c$ (no. 14), $a = 7.1609(3)$ Å, $b = 4.6329(2)$ Å, $c = 30.0028(14)$ Å, $\beta = 96.635(4)°$, $V = 988.70(8)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0708$, $wR_{ref}(F^2) = 0.1761$, $T = 100.01(10)$ K.

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The crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.12 × 0.11 mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ:	0.90 mm^{-1}
Diffractometer, scan mode:	SuperNova, ω
θ_{max}, completeness:	73.6°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6711, 1970, 0.088
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 1675
$N(param)_{refined}$:	140
Programs:	CrylAlis^{PRO} [1], SHELX [2], OLEX2 [3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	x	y	z	U_{iso}*/U_{eq}
O1	−0.01846(18)	0.4873(3)	0.66901(4)	0.0196(4)
O2	0.1203(2)	0.9075(3)	0.74657(4)	0.0235(4)
O3	0.3821(2)	1.1300(3)	0.73017(4)	0.0209(4)
O4	0.38588(18)	0.5412(3)	0.55439(4)	0.0185(4)
C1	0.1363(2)	0.6048(4)	0.65413(6)	0.0148(4)
H1	−0.020422	0.528186	0.695542	0.029*
C2	0.1804(2)	0.5184(4)	0.61185(6)	0.0153(4)
C3	0.3416(3)	0.6327(4)	0.59606(6)	0.0151(4)
C4	0.4642(2)	0.8294(4)	0.62014(6)	0.0161(4)
C5	0.4117(3)	0.9143(4)	0.66116(6)	0.0162(4)
C6	0.2524(2)	0.8070(4)	0.67775(6)	0.0156(4)
C7	0.2367(3)	0.9435(4)	0.72097(6)	0.0179(4)
C8	0.5047(3)	1.1211(4)	0.69492(6)	0.0194(5)
H8A	0.629125	1.053572	0.706522	0.023*
H8B	0.515743	1.310691	0.681756	0.023*
C9	0.0550(3)	0.3052(4)	0.58486(6)	0.0190(4)
H9A	0.046987	0.131070	0.601891	0.028*
H9B	0.106325	0.262041	0.557449	0.028*
H9C	−0.068312	0.386552	0.578056	0.028*
C10	0.3057(3)	0.7226(5)	0.51866(6)	0.0263(5)
H10A	0.345020	0.657239	0.490854	0.040*
H10B	0.347119	0.917743	0.524256	0.040*
H10C	0.171070	0.714819	0.516886	0.040*
C11	0.6392(3)	0.9435(5)	0.60296(7)	0.0219(5)
H11A	0.615017	1.132848	0.590618	0.033*
H11B	0.675166	0.817026	0.580091	0.033*
H11C	0.738909	0.953508	0.627210	0.033*

***Corresponding author: Yi-Wen Tao,** Key Laboratory of Molecular Target and Clinical Pharmacology, School of Pharmaceutical Sciences and the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong 511436, P.R. China, e-mail: yywentao@aliyun.com
Pei-Wen Chen: Key Laboratory of Molecular Target and Clinical Pharmacology, School of Pharmaceutical Sciences and the Fifth Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong 511436, P.R. China

Source of material

All solvents were of analytical grade. The title compound was isolated from the mangrove endophytic fungi *Pestalotiopsis* sp. collected from Dongzhai Harbor of Hainan Island, China, further purified by reversed-phase HPLC using a Sharpsil-U 5 μm C18 100 Å column (10.00 × 250 mm) and an isocratic 50% acetonitrile/50% H_2O at the flowrate of 2 mL/min over 30 min, detection at 254 nm, and afforded 8.6 mg. Colorless crystals were obtained from slow evaporation of the methanol solution in open air at room temperature.

^{1}H-NMR(400 MHz, Methanol-D4)**:** 5.24 ppm (2H, s), 3.76 ppm (3H, s), 2.17 ppm (3H, s), 2.14 ppm (3H, s).

Experimental details

U_{iso} values of hydrogen atoms were set to $1.2U_{eq}$ of the parent atoms.

Comment

Pestalotiopsis sp. was isolated from the stem of mangrove *Sonneratia apetala* planted at Dongzhai Harbor of Hainan Island, China, and identified by 18S RNA gene sequence [4]. The strain was cultured and fermented using rice medium (rice 250 g/L, crude sea salt 2 g/L) on stable condition at 28 °C for 30 days as described in Zhang's paper [5]. Then the culture was repetitively extracted with MeOH solvent and fractionated using normal-phase vacuum liquid chromatography (VLC) to obtain nine fractions (Fr. A-I). Fraction E (50% hexanes/50% EtOAc) was further purified by reversed-phase HPLC, and 7-hydroxy-5-methoxy-4,6-dimethylphthalide was obtained. Its structure was elucidated by comprehensive analysis of spectroscopic data, and confirmed by single-crystal X-ray crystallography.

7-hydroxy-5-methoxy-4,6-dimethylphthalide, as a phthalide derivative, carry a lactone formed by dehydrationreaction of γ-hydroxy carboxylic acids. Phthalides have been possessing various biological activities such as antifugi, antibacteria, antivirus, antitumor, treatment of thrombosis and cerebral vascular diseases [6–8].

The title compound has been reported before from the same fungus, containing its ^{1}H-NMR and ^{13}C-NMR data, it also showed significant antiviral activities against Cox-B3 and RSV with IC_{50} values of 19.6 μM and 21.0 μM [9]. The crystal structure of title compound has not been reported before, however similar compounds have been identified by X-ray crystallographic diffraction analysis [10].

Furthermore, the crystal structure of the parent is known, in which all geometric parameters are in accord with the present study [11].

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