Crystal structure of (3*R*,4*S*)-6,8-dihydroxy-3,4,5-trimethyl-1-oxoisochroman-7-carboxylic acid, $C_{13}H_{14}O_6$

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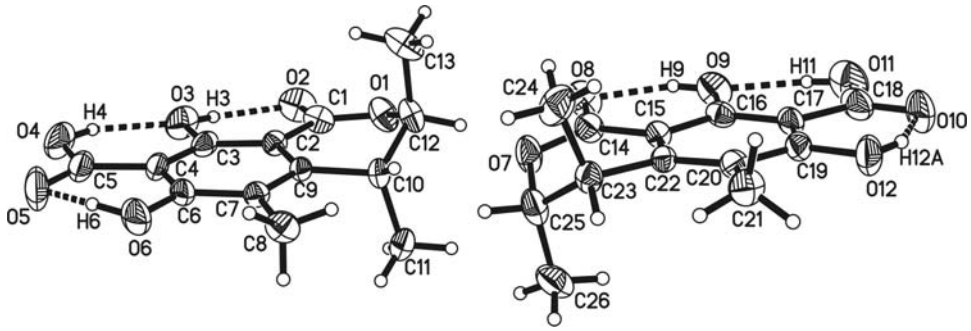

Abstract

$C_{13}H_{14}O_6$, orthorhombic, $P2_12_12_1$ (no. 19), a = 9.104(2) Å, b = 10.325(2) Å, c = 26.343(5) Å, V = 2476.1 Å^3, Z = 8, $R_{gt}(F)$ = 0.041, $wR_{ref}(F^2)$ = 0.121, T = 293 K.

Source of material

The isolated *Aspergillus terreus* originated from rhizosphere soil of *Lycopersicum esculentum* Mill (tomato), collected from Xuzhou, Jiangsu Province, China. The fresh mycelium of *A. terreus* grown on PDA medium at 28 °C for 5 days was inoculated into 1000 mL flasks containing 500 mL of PD medium. After 4-day incubation at 28 °C on a rotary shaker at 150 rpm, 15 mL of culture liquid was transferred as seed into wheat bran solid state fermentation media (millet 7.5 g, wheat bran 7.5 g, yeast extract 0.5 g, $FeSO_4 \cdot 7H_2O$ 0.01 g, sodium tartrate 0.1 g, sodium glutamate 0.1 g, corn oil 0.1 mL, water 15 mL in each bottle, autoclaved at 121 °C for 20 min). After 35 days' incubation at 28 °C, the crude solid fermentation products were extracted with $CHCl_3$/MeOH (1:1, *v*/*v*) at room temperature. Evaporation of the solvent in vacuo gave a black extract (300 g) after wax burnout and desalination of the extract with MeOH/H_2O (85:15, *v*/*v*) and MeOH/Me_2CO (85:15, *v*/*v*), respectively. The crude extract was subjected to chromatography over a silica gel column (1500 g, 200 - 300 mesh) eluting with $CHCl_3$/MeOH (1:0 - 0:1), to yield seven fractions. Fraction 1 (1:0 $CHCl_3$/MeOH isocratic) was further separated over a silica gel column with a $CHCl_3$/MeOH gradient to yield the title compound as white amorphous powder. Colorless block crystals were obtained by slow evaporation of a $CHCl_3$/MeOH (1:1, *v*/*v*) solution. The crystals were isolated, washed three times with chloroform and dried in a vacuum desiccator using P_4O_{10} (yield 46.7 %). Elemental analysis — found: C, 58.7 %; H, 5.3 %; O, 36.1 %; calculated for $C_{13}H_{14}O_6$: C, 58.6 %; H, 5.3 %; N, 36.0 %.

Experimental details

H atoms were positioned geometrically and constrained to ride on their parent atoms with d(C—H) distances of 0.96 - 0.98 Å and d(O—H) = 0.82 Å, and with U_{iso}(H) = 1.2 or 1.5 U_{eq}(C,O).

Discussion

In the soil environment, fungi are one of the many members of a cosmopolitan community characterized by complex interactions [1]. They play an important role for their effects on plants including beneficial associations in the rhizosphere, and also represent a valuable resource in the search for secondary metabolites with useful therapeutic applications [2,3]. Within our screening program for isolation of microorganisms containing bioactive components [4], a strain of *Aspergillus terreus* was isolated from the rhizosphere soil of tomato. The title compound, dihydrocitrinone, was first described by [5], and elucidated on the basic of spectroscopic analysis [6,7]. Herein, the compound was re-isolated from the solid fermentation culture of the soil-borne fungus *A. terreus*.

In the title crystal structure, all bond lengths are within normal ranges [8]. The strong intramolecular O–H···O hydrogen bond results in the formation of pseudo-six-membered planar rings, B(C1/C2/C3/O3/H3/O2), C(C3/C4/C5/O4/H4/O3) and D(C5/C4/C6/O6/H6/O5). The rings A(C2-C4/C6/C7/C9), B, C and D are each coplanar. The dihedral angles between the rings are 3.9(5)° between A and B, 2.1(3)° between A and C and 1.3(3)° between A and D, respectively. In the crystal packing, dipole-dipole and van der Waals interactions are effective in the molecular packing.

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Table 1. Data collection and handling.

Crystal:	colorless block, size 0.15 × 0.30 × 0.45 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.14 cm^{-1}
Diffractometer, scan mode:	Bruker SMART CCD, ω
$2\theta_{max}$:	55.16°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	21468, 3241
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2794
$N(param)_{refined}$:	359
Programs:	SHELXS-97 [9], SHELXL-97 [10], SHELXTL [11]

Table 2. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{iso}
H(8A)	4*a*	0.5651	0.0212	0.9655	0.088
H(8B)	4*a*	0.5546	0.0890	0.9124	0.088
H(8C)	4*a*	0.5895	–0.0594	0.9158	0.088
H(10)	4*a*	0.3990	0.2214	0.8974	0.054
H(11A)	4*a*	0.3829	0.2327	0.9867	0.104
H(11B)	4*a*	0.2177	0.2742	0.9826	0.104
H(11C)	4*a*	0.3415	0.3668	0.9627	0.104
H(12)	4*a*	0.2074	0.3743	0.8815	0.070
H(13A)	4*a*	0.1265	0.2875	0.8051	0.117
H(13B)	4*a*	0.1858	0.1509	0.8209	0.117
H(13C)	4*a*	0.2958	0.2650	0.8113	0.117
H(21A)	4*a*	1.0484	0.6655	0.7809	0.090
H(21B)	4*a*	1.0446	0.6023	0.8350	0.090
H(21C)	4*a*	1.0764	0.7508	0.8292	0.090
H(23)	4*a*	0.8916	0.4770	0.8611	0.056
H(24A)	4*a*	0.7106	0.3942	0.7797	0.111
H(24B)	4*a*	0.8331	0.3086	0.8046	0.111
H(24C)	4*a*	0.8763	0.4328	0.7738	0.111
H(25)	4*a*	0.7046	0.3291	0.8861	0.072
H(26A)	4*a*	0.6156	0.4426	0.9558	0.116
H(26B)	4*a*	0.6737	0.5725	0.9325	0.116
H(26C)	4*a*	0.7849	0.4650	0.9495	0.116
H(3)	4*a*	–0.1214	–0.0539	0.9297	0.111
H(4)	4*a*	–0.0508	–0.2936	0.9400	0.153
H(9)	4*a*	0.3639	0.7303	0.8193	0.100
H(11)	4*a*	0.4267	0.9675	0.8000	0.151
H(12A)	4*a*	0.8741	0.9923	0.7925	0.110
H(6)	4*a*	0.3640	–0.3060	0.9450	0.140

Table 3. Atomic coordinates and displacement parameters (in $Å^2$).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	4*a*	0.0019(3)	0.1373(3)	0.91004(9)	0.041(1)	0.066(2)	0.051(1)	0.009(1)	0.005(1)	0.003(1)
C(2)	4*a*	0.1159(2)	0.0397(2)	0.91904(8)	0.040(1)	0.041(1)	0.042(1)	–0.0020(9)	0.0024(8)	–0.0003(9)
C(3)	4*a*	0.0737(3)	–0.0881(2)	0.92944(9)	0.053(1)	0.052(1)	0.043(1)	–0.021(1)	0.004(1)	–0.004(1)
C(4)	4*a*	0.1777(4)	–0.1839(2)	0.93786(9)	0.080(2)	0.034(1)	0.044(1)	–0.012(1)	0.004(1)	–0.0031(9)
C(5)	4*a*	0.1397(5)	–0.3214(3)	0.9473(1)	0.132(3)	0.044(2)	0.051(1)	–0.024(2)	0.007(2)	–0.003(1)
C(6)	4*a*	0.3279(3)	–0.1486(2)	0.93727(9)	0.068(2)	0.036(1)	0.042(1)	0.007(1)	–0.001(1)	0.0001(9)
C(7)	4*a*	0.3732(3)	–0.0194(2)	0.92872(8)	0.044(1)	0.040(1)	0.040(1)	0.002(1)	–0.0011(9)	–0.0009(9)
C(8)	4*a*	0.5354(3)	0.0106(3)	0.9308(1)	0.041(1)	0.070(2)	0.065(1)	0.006(1)	–0.005(1)	0.006(1)
C(9)	4*a*	0.2665(2)	0.0722(2)	0.91970(7)	0.039(1)	0.0317(9)	0.0361(9)	–0.0041(8)	0.0014(8)	0.0017(8)
C(10)	4*a*	0.3025(3)	0.2144(2)	0.91360(9)	0.048(1)	0.034(1)	0.054(1)	–0.007(1)	0.004(1)	0.0069(9)
C(11)	4*a*	0.3120(4)	0.2780(3)	0.9664(1)	0.096(2)	0.041(1)	0.071(2)	–0.013(2)	–0.004(2)	–0.007(1)
C(12)	4*a*	0.1900(3)	0.2808(3)	0.8794(1)	0.060(2)	0.047(1)	0.068(2)	0.008(1)	0.009(1)	0.020(1)
C(13)	4*a*	0.2005(4)	0.2426(4)	0.8241(1)	0.073(2)	0.104(2)	0.057(1)	0.019(2)	0.006(1)	0.028(2)
C(14)	4*a*	0.4929(3)	0.5475(3)	0.84321(9)	0.043(1)	0.056(1)	0.056(1)	–0.006(1)	–0.003(1)	0.009(1)
C(15)	4*a*	0.6036(2)	0.6448(2)	0.83151(8)	0.038(1)	0.040(1)	0.041(1)	0.0004(9)	0.0005(8)	0.0055(9)
C(16)	4*a*	0.5570(3)	0.7690(2)	0.81749(8)	0.047(1)	0.048(1)	0.040(1)	0.012(1)	–0.0013(9)	0.0023(9)
C(17)	4*a*	0.6599(3)	0.8656(2)	0.80702(9)	0.072(2)	0.034(1)	0.041(1)	0.006(1)	0.002(1)	0.0026(9)
C(18)	4*a*	0.6179(4)	1.0004(3)	0.7943(1)	0.111(3)	0.046(1)	0.055(1)	0.015(2)	–0.002(2)	0.005(1)
C(19)	4*a*	0.8098(3)	0.8338(2)	0.80842(8)	0.062(1)	0.041(1)	0.040(1)	–0.009(1)	0.008(1)	0.0001(9)
C(20)	4*a*	0.8591(3)	0.7068(2)	0.81941(8)	0.043(1)	0.045(1)	0.041(1)	–0.003(1)	0.0040(9)	0.0002(9)
C(21)	4*a*	1.0220(3)	0.6788(3)	0.8158(1)	0.040(1)	0.073(2)	0.066(1)	–0.008(1)	0.009(1)	0.000(1)
C(22)	4*a*	0.7547(2)	0.6152(2)	0.83210(7)	0.038(1)	0.034(1)	0.0386(9)	0.0005(9)	0.0004(8)	0.0001(8)
C(23)	4*a*	0.7948(3)	0.4769(2)	0.84482(9)	0.042(1)	0.037(1)	0.061(1)	0.005(1)	–0.006(1)	0.005(1)
C(24)	4*a*	0.8046(4)	0.3955(3)	0.7962(1)	0.076(2)	0.052(2)	0.095(2)	0.012(2)	–0.004(2)	–0.021(2)
C(25)	4*a*	0.6837(3)	0.4218(3)	0.8825(1)	0.051(1)	0.048(1)	0.082(2)	–0.002(1)	–0.007(1)	0.025(1)
C(26)	4*a*	0.6901(4)	0.4808(4)	0.9348(1)	0.068(2)	0.102(2)	0.062(2)	–0.013(2)	–0.005(1)	0.033(2)
O(1)	4*a*	0.0401(2)	0.2566(2)	0.89721(8)	0.058(1)	0.060(1)	0.076(1)	0.0222(9)	0.0104(9)	0.0171(9)
O(2)	4*a*	–0.1304(2)	0.1126(3)	0.91457(9)	0.0373(9)	0.107(2)	0.084(1)	0.008(1)	0.0063(9)	0.004(1)
O(3)	4*a*	–0.0717(2)	–0.1200(2)	0.93090(9)	0.057(1)	0.085(1)	0.081(1)	–0.036(1)	0.005(1)	–0.002(1)
O(4)	4*a*	0.0010(4)	–0.3572(2)	0.9453(1)	0.152(3)	0.069(2)	0.086(2)	–0.065(2)	0.005(2)	0.002(1)
O(5)	4*a*	0.2321(5)	–0.4035(2)	0.9557(1)	0.182(3)	0.036(1)	0.102(2)	–0.004(2)	0.014(2)	0.009(1)
O(6)	4*a*	0.4338(3)	–0.2369(2)	0.94488(9)	0.097(2)	0.050(1)	0.078(1)	0.027(1)	–0.005(1)	0.005(1)
O(7)	4*a*	0.5343(2)	0.4338(2)	0.86239(8)	0.049(1)	0.055(1)	0.093(1)	–0.0172(9)	–0.0087(9)	0.027(1)
O(8)	4*a*	0.3608(2)	0.5651(2)	0.83633(9)	0.0368(9)	0.095(2)	0.092(1)	–0.010(1)	–0.0056(9)	0.028(1)
O(9)	4*a*	0.4116(2)	0.7964(2)	0.81437(9)	0.050(1)	0.071(1)	0.078(1)	0.023(1)	–0.005(1)	0.011(1)
O(10)	4*a*	0.7091(4)	1.0849(2)	0.7860(1)	0.154(3)	0.040(1)	0.101(2)	–0.006(2)	–0.005(2)	0.017(1)
O(11)	4*a*	0.4761(3)	1.0309(2)	0.7923(1)	0.125(2)	0.063(2)	0.113(2)	0.045(2)	–0.007(2)	0.015(1)
O(12)	4*a*	0.9133(3)	0.9227(2)	0.79877(9)	0.088(2)	0.053(1)	0.078(1)	–0.027(1)	0.013(1)	0.009(1)

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References

1. Cazar, M. E.; Schmeda-Hirschmann, G.; Astudillo L.: Antimicrobial butyrolactone I derivatives from the ecuadorian soil fungus Aspergillus terreus thorn. Var terreus World. J. Microb. Biotechnol. **21** (2005) 1067-1075.
2. Takahashi, K.; Koshino, H.; Narita, Y.; Yoshihara, T.: Novel antifungal compounds produced by Sterile Dark, an unidentified wheat rhizosphere fungus. Biosci. Biotechnol. Biochem. **69** (2005) 1018-1020.
3. Wijeratne, E. M. K.; Turbyville, T. J.; Zhang, Z. G.; Bigelow, D.; Pierson, L. S.; Van Etten, H. D.; Whitesell, L.; Canfield, L. M.; Gunatilaka, A. A. L.: Cytotoxic constituents of Aspergillus terreus from the rhizosphere of Opuntia versicolor of the Sonoran desert. J. Nat. Prod. **66** (2003) 1567-1573.
4. Xue, Q. Y.; Chen, Y.; Li, S. M.; Chen, L. F.; Ding, G. C.; Guo, D. W.; Guo, J. H.: Evaluation of the strains of Acinetobacter and Enterobacter as potential biocontrol agents against Ralstonia wilt of tomato. Biol. Control **48** (2009) 252-258.
5. Hassall, C. H.; Jones, D. W.: The biosynthesis of phenols. IV. A new metabolic product of Aspergillus terreus. J. Chem. Soc. (1962) 4189-4191.
6. Chien, M. M.; Schiff, P. L.; Slatkin, D. J.; Knapp, J. E.: Metabolites of aspergilli.3. isolation of citrinin, dihydrocitrinone and sclerin from Aspergillus-carneus. Lloydia **40** (1977) 301-302.
7. Xin, Z. H.; Tian, L.; Zhu, T. J.; Wang, W. L.; Du, L.; Fang, Y. C.; Gu, Q. Q.; Zhu, W. M.: Isocoumarin derivatives from the sea squirt-derived fungus Penicillium stoloniferum QY2-10 and the halotolerant fungus Penicillium notatum B-52. Arch. Pharm. Res. **30** (2007) 816-819.
8. Cheng, K.; You, Z. L.; Li, Y. G.; Zhu, H. L.: 2-(*o*-Tolyliminomethyl)phenol. Acta. Crystallogr. **E61** (2005) o1137-o1138.
9. Sheldrick, G. M.: SHELXS-97. Program for the Solution of Crystal Structures. University of Göttingen, Germany 1997.
10. Sheldrick, G. M.: SHELXL-97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany 1997.
11. Sheldrick, G. M.: SHELXTL. Structure Determination Software Suite. Version 6.14. Bruker AXS, Madison, Wisconsin, USA 2000.