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The crystal structure of (2*R*,6'*R*)-2',7-dichloro-4,6-dimethoxy-6'-methyl-3*H*-spiro[benzofuran-2,1'-cyclohexan]-2'-ene-3,4'-dione, C₁₆H₁₄Cl₂O₅

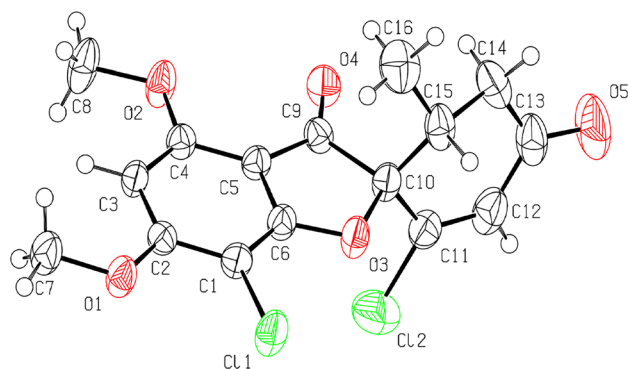


Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.18 × 0.14 × 0.12 mm
Wavelength:	Cu Kα radiation (1.54184 Å)
μ:	3.73 mm ⁻¹
Diffractometer, scan mode:	Xcalibur, ω
θ _{max} , completeness:	71.7°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	13,604, 6350, 0.037
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2σ(<i>I</i> _{obs}), 5967
<i>N</i> (<i>param</i>) _{refined} :	421
Programs:	Olex2 [1], SHELX [2, 3]

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Abstract

C₁₆H₁₄Cl₂O₅, orthorhombic, *P*2₁2₁2₁ (no. 19), *a* = 23.2297(5) Å, *b* = 16.3509(3) Å, *c* = 8.7300(2) Å, *V* = 3315.89(12) Å³, *Z* = 8, *R*_{gt}(*F*) = 0.0472, *wR*_{ref}(*F*²) = 0.1268, *T* = 293 K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of materials

2'-Hydroxy-griseofulvin (339 mg, 1.0 mmol) was mixed with LiCl (212 mg, 5 mmol) and added to a solution of phosphorylchloride (0.56 mL, 5 mmol) in dioxane (28 mL). The mixture was refluxed for 30 min, cooled to room

temperature and sat. aq. sodium carbonate was added carefully to the solution until it is slightly basic (pH 7–8). The aqueous phase was extracted with DCM (3 × 20 mL) and the combined organic phases were dried (sodium sulfate anhydrous) and concentrated. The residue was purified by column chromatography DCM and the white solid (121 mg) was obtained, yield 34%. This white solid is recrystallized to obtain colorless crystals from solution (DCM: methanol 5:1) by natural cooling method at room temperature.

Experimental details

Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program and refined with the SHELXL [3] refinement package. All hydrogen atomic positions were taken from a difference Fourier map. Their *U*_{iso} values were set to 1.2*U*_{eq} (C, phenyl ring and methylene), 1.5*U*_{eq} (C, methyl) of the parent atoms, respectively. All the H atoms were refined as riding on their parent atom.

Comment

Griseofulvin is a very important natural product [4]. Several hundreds of griseofulvin analogues have been synthesized and used for drug screening since it was isolated [5, 6]. In this paper, one analogue of griseofulvin (2*R*,6'*R*)-2',7-dichloro-4,6-dimethoxy-6'-methyl-3*H*-spiro[benzo-furan-2,1'-cyclohexan]-2'-ene-3,4'-dione was synthesized by using 2'-hydroxy-griseofulvin as starting material, and the structure was determined by

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C1	0.40390(16)	−0.0359(2)	0.3024(5)	0.0383(8)
C2	0.46077(15)	−0.0267(2)	0.2525(5)	0.0346(7)
C3	0.48246(15)	0.0506(2)	0.2135(4)	0.0343(7)
H3	0.520322	0.055705	0.180311	0.041 [*]
C4	0.44787(15)	0.1192(2)	0.2242(4)	0.0322(7)
C5	0.39040(15)	0.1105(2)	0.2717(4)	0.0321(7)
C6	0.37012(15)	0.0327(2)	0.3097(5)	0.0363(8)
C7	0.54806(17)	−0.0951(3)	0.1820(6)	0.0509(11)
H7A	0.546491	−0.077225	0.077337	0.076 [*]
H7B	0.564181	−0.149142	0.186367	0.076 [*]
H7C	0.571688	−0.058282	0.240103	0.076 [*]
C8	0.52393(18)	0.2093(2)	0.1544(7)	0.0574(13)
H8A	0.535481	0.174017	0.071973	0.086 [*]
H8B	0.546724	0.197601	0.243439	0.086 [*]
H8C	0.529489	0.265261	0.124763	0.086 [*]
C9	0.34326(15)	0.1668(2)	0.2905(5)	0.0328(7)
C10	0.29049(15)	0.1126(2)	0.3358(5)	0.0372(8)
C11	0.26557(17)	0.1391(3)	0.4848(6)	0.0451(9)
C12	0.2162(2)	0.1780(3)	0.5020(7)	0.0550(11)
H12	0.204246	0.193094	0.599749	0.066 [*]
C13	0.17962(19)	0.1981(3)	0.3694(8)	0.0569(13)
C14	0.20421(19)	0.1822(3)	0.2165(7)	0.0547(12)
H14A	0.225309	0.230263	0.183583	0.066 [*]
H14B	0.172932	0.173711	0.144611	0.066 [*]
C15	0.24466(16)	0.1079(2)	0.2097(6)	0.0446(10)
H15	0.221220	0.059311	0.230385	0.054 [*]
C16	0.2709(2)	0.0969(4)	0.0513(6)	0.0616(13)
H16A	0.293218	0.144340	0.025514	0.092 [*]
H16B	0.240778	0.089761	−0.022717	0.092 [*]
H16C	0.295357	0.049500	0.051236	0.092 [*]
C17	0.66929(16)	0.0863(2)	0.4327(4)	0.0351(7)
C18	0.72523(16)	0.1037(2)	0.4822(4)	0.0355(7)
C19	0.73864(15)	0.1058(2)	0.6388(5)	0.0363(8)
H19	0.776000	0.117820	0.669699	0.044 [*]
C20	0.69723(15)	0.0901(2)	0.7469(4)	0.0338(7)
C21	0.64078(15)	0.0717(2)	0.6988(4)	0.0336(7)
C22	0.62859(16)	0.0698(2)	0.5414(4)	0.0332(7)
C23	0.82307(18)	0.1290(4)	0.4123(6)	0.0584(12)
H23A	0.845972	0.133296	0.321175	0.088 [*]
H23B	0.835864	0.082962	0.471627	0.088 [*]
H23C	0.827038	0.178016	0.471817	0.088 [*]
C24	0.76241(17)	0.1103(3)	0.9552(5)	0.0438(9)
H24A	0.773212	0.164242	0.922567	0.066 [*]
H24B	0.789254	0.071202	0.914964	0.066 [*]
H24C	0.762710	0.107868	1.065104	0.066 [*]
C25	0.58832(16)	0.0531(2)	0.7792(4)	0.0349(8)
C26	0.54234(15)	0.0390(2)	0.6512(4)	0.0361(7)
C27	0.51962(17)	−0.0476(2)	0.6617(5)	0.0440(9)
C28	0.4701(2)	−0.0679(3)	0.7276(7)	0.0586(12)
H28	0.459790	−0.122781	0.732555	0.070 [*]
C29	0.43118(19)	−0.0062(3)	0.7929(7)	0.0581(12)
C30	0.45238(17)	0.0802(3)	0.7912(5)	0.0472(9)

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
H30A	0.473358	0.090667	0.885295	0.057 [*]
H30B	0.419546	0.116810	0.788791	0.057 [*]
C31	0.49141(15)	0.0992(2)	0.6553(5)	0.0403(8)
H31	0.468818	0.090511	0.561876	0.048 [*]
C32	0.5103(2)	0.1886(3)	0.6564(7)	0.0568(11)
H32A	0.529294	0.200624	0.751493	0.085 [*]
H32B	0.477227	0.223261	0.645408	0.085 [*]
H32C	0.536412	0.198228	0.572978	0.085 [*]
Cl1	0.37635(4)	−0.13056(6)	0.34976(17)	0.0577(3)
Cl2	0.30846(7)	0.11896(12)	0.64266(17)	0.0796(4)
Cl3	0.65267(4)	0.08270(7)	0.23957(10)	0.0477(3)
Cl4	0.56517(6)	−0.12275(7)	0.59112(17)	0.0619(3)
O1	0.49127(11)	−0.09623(16)	0.2447(4)	0.0467(7)
O2	0.46417(12)	0.19569(15)	0.1887(4)	0.0477(8)
O3	0.31403(11)	0.03064(15)	0.3511(4)	0.0455(7)
O4	0.34021(12)	0.24051(15)	0.2743(4)	0.0433(7)
O5	0.13290(16)	0.2295(3)	0.3889(7)	0.0880(16)
O6	0.76356(12)	0.1178(2)	0.3710(3)	0.0490(7)
O7	0.70581(12)	0.0919(2)	0.9002(3)	0.0440(7)
O8	0.57301(11)	0.05116(18)	0.5083(3)	0.0392(6)
O9	0.57786(12)	0.0478(2)	0.9153(3)	0.0475(7)
O10	0.38514(17)	−0.0251(3)	0.8469(7)	0.0958(17)

X-ray single crystal diffraction. It is a key chemical intermediate which was used for preparation of the 2'-modified griseofulvin analogues [7, 8].

The asymmetric unit of the title structure contains two crystallographically independent molecules, and one of these molecules is shown in the figure. In the molecule, the bond length of Cl1–C1 is 1.725(4) Å. The angle of O11–C10–C15 is 111.8(3)°, the bond lengths and angles of the title compound are similar to the structure of natural product griseofulvin [9] and a related structure [10]. The plane (C5/C6/C1) of benzene ring and the plane (C6/C5/C9) of furan ring are approximately in the same plane and their dihedral angle is only 0.87°. The plane (C10/O3/C9) of furan ring and the plane (C10/C11/C15) of cyclohexanone present a dihedral angle of about 88.13°. Cyclohexanone ring (C10/C11/C12/C13/C14/C15) has a half-chair conformation. The crystal packing exhibits weak intermolecular C–H...O interactions and C–H...Cl hydrogen bonds.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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