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An orthorhombic modification of (*R*)-(−)-8-hydroxy-3-methyl-3,4-dihydro-1*H*-2-benzopyran-1-one [(*R*)-(−)-mellein]

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.003 Å
R factor = 0.046
wR factor = 0.110
Data-to-parameter ratio = 9.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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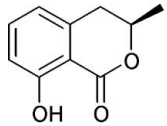
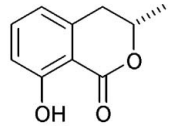
In addition to the known triclinic modification of the title compound, an orthorhombic modification is now described. In the crystal packing of the title compound, $C_{10}H_{10}O_3$, the molecules are linked *via* intermolecular C–H···O hydrogen bonds into infinite chains which extend in the [100] direction and are stacked along [001].

Comment

The title compound, (*R*)-(−)-mellein, is a naturally occurring dihydroisocoumarin which was first isolated as a metabolite of *Aspergillus melleus* (Nishikawa, 1933*a*,*b*). Since then, the compound has been found in many fungal cultures (for a review, see Hill, 1986) and several insects (for a review, see Gill, 1993), in which it appears to play a pheromonal role. More recently, it has been isolated from the fungus *Phomopsis oblonga* (Claydon *et al.*, 1985), *Microsphaeropsis* sp. from the marine sponge *M. incrustans* (Höller *et al.*, 1999), and *Aspergillus ochraceus* (Dai, *et al.*, 2001). In our group, we have isolated (*R*)-(−)-mellein from a number of endophytic fungi, such as *Pezicula livida*, *Plectophomella* sp., and *Cryptosporiopsis malicoticis* (Krohn *et al.* 1997), and recently from *Geniculosporium* sp., a fungus that is associated with the red alga *Polysiphonia* sp., isolated from the Baltic Sea at Ahrenshoop, and an unidentified endophytic fungus, which was isolated from the plant *Angelica archangelica* (Umbelliferae) from Bodstetter Bodden, Baltic Sea. It is biosynthetically derived from a pentaketide (Abell *et al.*, 1983) and also occurs in nature as the enantiomer (*S*)-(+)-mellein (see scheme), also named ochracin, isolated from *Fusarium larvarum* and showing insecticidal activity (Grove & Pople, 1979), and the marine fungus *Helicascus kanaloanus* (Poch & Gloer, 1989). (*R*)-(−)-Mellein shows a number of interesting biological activities (for a review, see Cole & Cox, 1981), such as fungicidal, antibacterial and algicidal activity in agar diffusion tests (Krohn *et al.* 1997, Höller *et al.*, 1999), and it inhibits HCV protease with an IC_{50} value of 35 μ*M*, but it has been found to be inactive against HIV-1 reverse transcriptase (Dai *et al.*, 2001).



(*R*)-(−)-mellein



(*S*)-(+)-mellein

(I)

Despite its long history, the first crystallographic characterization of mellein was performed only recently (Efdi *et*

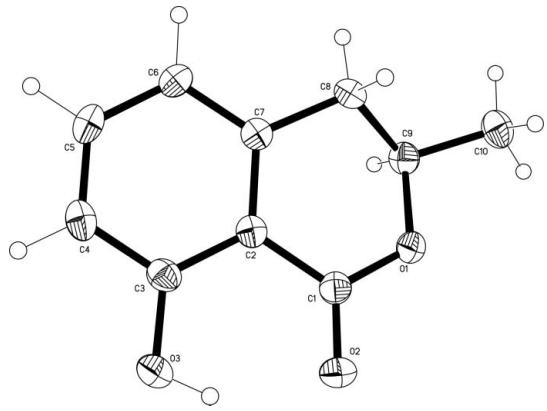


Figure 1
The molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

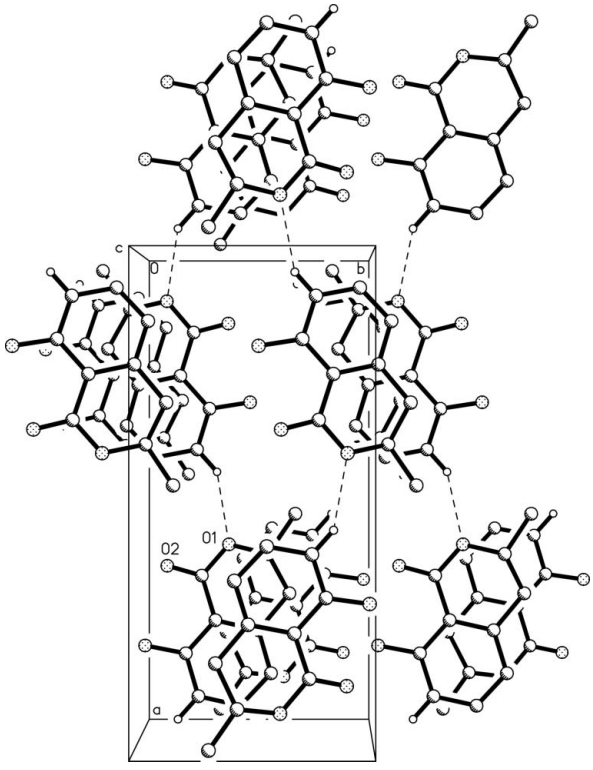


Figure 2
The packing, viewed along [001], with intermolecular hydrogen bonds indicated by dashed lines. H atoms not involved in hydrogen bonding have been omitted.

al., 2006), reporting a triclinic cell, space group $P1$ (No. 1), with six independent molecules in the asymmetric unit. Our data now confirm a new modification, orthorhombic, $P2_12_12_1$, with one molecule per asymmetric unit. The molecular structure (Fig. 1) is similar to that of 3,8-dihydroxy-3-methyl-3,4-dihydroisocoumarin (Kawai *et al.*, 1985), with the same half-chair conformation of the dihydropyran ring and the methyl group in an equatorial position. All geometric parameters lie in expected ranges (Kawai *et al.*, 1985) and thus need no further detailed discussion.

An intramolecular O–H···O hydrogen bond is formed (Table 2) and the crystal structure (Fig. 2) shows intermolecular C–H···O interactions (Table 2), which link the molecules into infinite chains in the *a*-axis direction and stacks along [001].

Experimental

The culture broth of the unidentified endophytic fungus, isolated from the plant *Angelica archangelica* (Umbelliferae) (Schulz *et al.*, 2002), was extracted five times with ethyl acetate then filtered through a pad of anhydrous Na_2SO_4 and evaporated until complete dryness to afford 19.63 g of the crude extract. The extract was separated by silica-gel column chromatography, using petroleum ether–dichloromethane (1:1) and then by mixtures of up to 20% methanol in dichloromethane, which resulted in the isolation of pure mellein (0.21 g) as colourless crystals (0.21 g, m.p. 328 K). $[\alpha]_D$ = −67.7 (*c* 0.0027, MeOH, 295 K). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (1H, *dd*, J = 8.4 Hz, H-6), 6.92 (*d*, 1H, J = 8.4 Hz, H-5), 6.71 (*d*, 1H, J = 8.4 Hz, H-7), 4.67 (1H, *m*, H-3), 2.95 (*d*, 2H, J = 7.6 Hz, H-4), 1.55 (*d*, 3H, J = 6.3 Hz, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9 (C-1), 162.2 (C-8), 139.3 (C-4a), 136.1 (C-6), 117.8 (C-5), 116.2 (C-7), 108.3 (C-8a), 76.0 (C-3), 34.6 (C-4), 20.7 (Me).

Crystal data

$C_{10}H_{10}O_3$	Z = 4
M_r = 178.18	D_x = 1.419 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation
a = 15.193 (4) Å	μ = 0.11 mm^{-1}
b = 7.280 (2) Å	T = 120 (2) K
c = 7.538 (2) Å	Block, colourless
V = 833.8 (4) Å^3	0.45 × 0.31 × 0.25 mm

Data collection

Bruker SMART CCD area-detector diffractometer	7657 measured reflections
	1194 independent reflections
φ and ω scans	1073 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan *SADABS* (Bruker, 2002)	R_{int} = 0.052
	θ_{max} = 28.1°
T_{min} = 0.954, T_{max} = 0.978	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.058P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.046	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.110	$\Delta\rho_{max}$ = 0.24 e Å^{-3}
S = 1.25	$\Delta\rho_{min}$ = −0.17 e Å^{-3}
1194 reflections	Extinction correction: *SHELXL97*
120 parameters	Extinction coefficient: 0.009 (2)
H-atom parameters constrained	

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O2	0.84	1.84	2.572 (2)	145
C4—H4A···O1^{i}	0.95	2.50	3.285 (3)	140

Symmetry code: (i) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$.

H atoms were located in difference syntheses and refined as riding in their idealized positions, O—H = 0.84, C—H = 0.95–1.00 Å, with isotropic displacement parameters U_{iso}(H) = 1.2U_{eq}(C) or

$1.5U_{eq}$(methyl-C and hydroxyl group). Methyl H atoms were refined on the basis of rigid groups allowed to rotate but not tip. The title compound crystallizes in the non-centrosymmetric space group $P2_12_12_1$; however, in the absence of significant anomalous scattering effects, the Flack (1983) parameter is essentially meaningless. Accordingly, Friedel pairs were merged. The absolute configuration chosen is in accordance with the optical rotation data.

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2002); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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