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Crystal structure of 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-8-methylchroman-4-one, $C_{17}H_{16}O_5$

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Abstract

$C_{17}H_{16}O_5$, monoclinic, $P2_1/c$ (no. 14), a = 4.76512(14) Å, b = 16.0383(4) Å, c = 9.4922(3) Å, β = 101.161(3)°, V = 711.72(4) Å^3, Z = 2, $R_{gt}(F)$ = 0.0362, $wR_{ref}(F^2)$ = 0.0976, T = 296.15 K.

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Table 1 contains the crystallographic data. The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

1 Source of materials

The target compound, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-8-methylchroman-4-one (abbreviated as the chroman-4-one derivative), was purchased from Jilin Chinese Academy of Sciences – Yanshen Technology Co., Ltd. Its isolation and purification were performed based on general procedures for flavonoid compounds.[5,6] The dried and powdered plant material was first macerated with n-hexane at room temperature to thoroughly remove non-polar components such as lipids and pigments. The resulting defatted plant residue was air-dried and then exhaustively extracted with ethyl acetate. The combined ethyl acetate extracts were concentrated in vacuo to afford a dark, paste-like crude extract. This crude extract was dry-loaded onto a silica gel column and subjected to elution with an N-hexane/ethyl acetate phase (95:5, v/v). Fractions were monitored, and similar fractions containing the target product were combined. After concentration, the enriched fraction was subjected to final purification by preparative thin-layer chromatography using a phase of dichloromethane/methanol (95:5, v/v). The target band was scraped from the plate and eluted with methanol or ethyl acetate. Concentration of the eluate yielded the high-purity target compound. The purified powder was dissolved in a minimal amount of hot ethyl acetate to form a saturated solution. The hot solution was filtered into a clean tube, the mouth of which was then sealed with Parafilm. Several small holes were pierced to allow for slow evaporation of the solvent. The apparatus was left undisturbed at room temperature, yielding colorless, block crystals in approximately one week.

2 Experimental details

A quality crystal of the title compound was collected using single-crystal X-ray diffraction analysis. The crystal structure was initially solved by employing Direct Methods within the Shelxt program. Subsequently, the structural model was refined using the Shelxl program through a full-matrix least-squares minimization on F^2. All non-hydrogen atoms (C and O) were refined with anisotropic displacement parameters, whereas hydrogen atoms were placed in geometrically calculated positions and refined isotropically.

3 Comment

The chroman-4-one scaffold, a bicyclic heterocycle composed of a benzene ring with a ketone-bearing dihydropyran ring, is a privileged scaffold of fundamental importance in organic and medicinal chemistry. It not only forms the core structure of numerous natural products, such as flavonoids, but also serves as a highly versatile synthetic building block.[7–12] Consequently, its derivatives exhibit a broad spectrum of biological activities including anticancer, antioxidant, and anti-inflammatory properties, making it a pivotal intermediate for the design and discovery of novel lead compounds in drug development. Although the crystal structures of numerous chroman-4-one derivatives have been reported, that of 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-8-methylchroman-4-one has remained unreported. Single-crystal X-ray diffraction test proved that the

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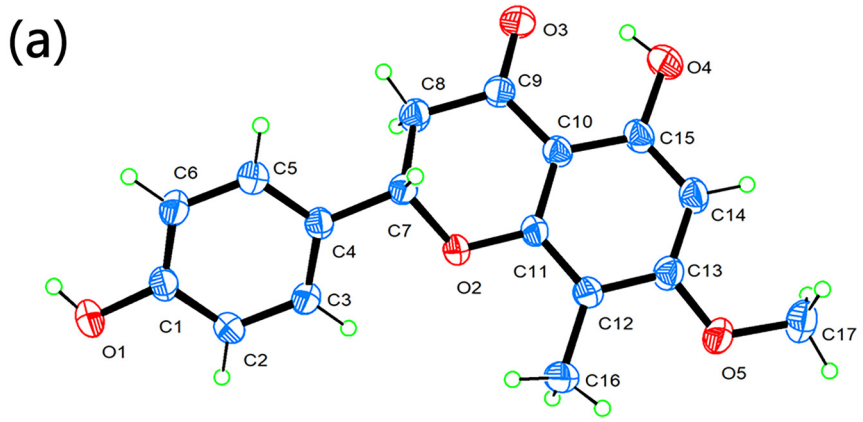

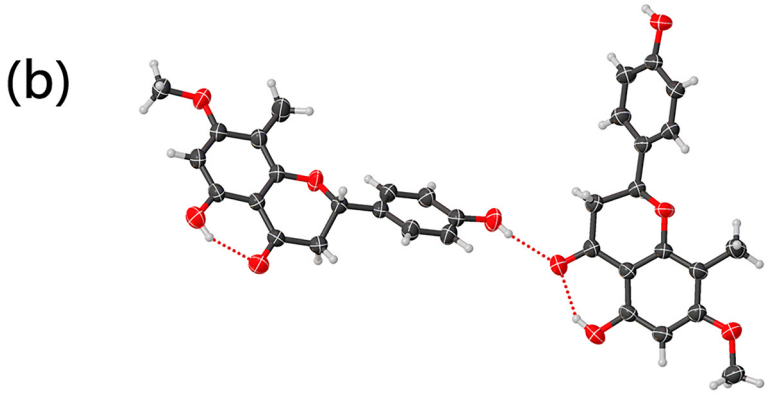

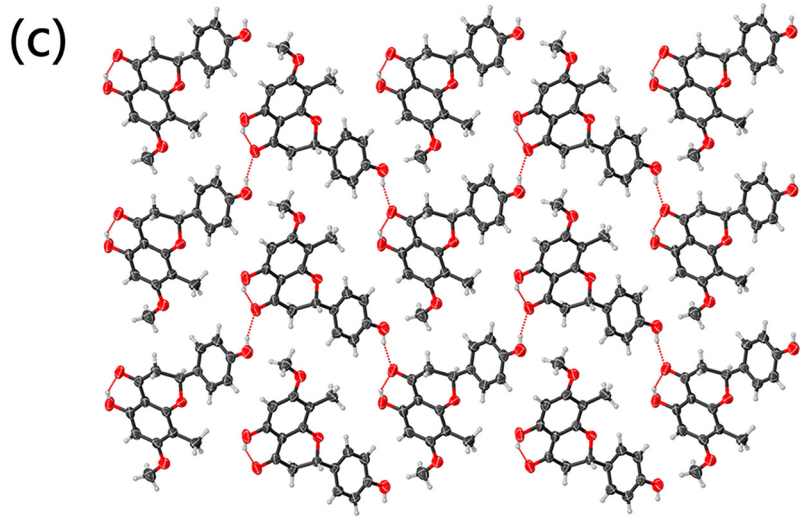

title chroman-4-one derivative crystallizes in the monoclinic crystal system belonging to the $P2_1/c$ space group. The asymmetric unit contains one complete chroman-4-one derivative molecule (see the figure, part a). The C–C bond lengths in the crystal are observed to be in the range of 1.374(4) Å to 1.518(3) Å, with the shortest and longest bonds being C14–C15 and C7–C8, respectively. Meanwhile, the C–O bond lengths vary from 1.258(3) Å to 1.437(3) Å, corresponding to the C9–O3 and C7–O2 bonds, respectively. These bond lengths are similar to the reported chroman-4-one derivatives.[13–18] The molecular structure of the chroman-4-one derivative can be regarded as comprising two principal

Table 1: Data collection and handling.

Crystal:	**Needle, clear light colourless**
Size:	0.19 × 0.18 × 0.15 mm
Wavelength:	Cu *Kα* radiation (1.54184 Å)
μ:	0.86 mm^{-1}
Diffractometer, scan mode:	Bruker SMART APEX-II, φ and ω-scans
θ_{max}, completeness:	74.1°, >99 %
N $(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	3732, 2,133, 0.023
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs}>2σ(I_{obs}), 1993
N (param)^{refined}:	203
Programs:	Bruker programs[1], OLEX2[2], SHELX[3,4]

moieties (hydrogen atoms are omitted for clarity in the following description). The first is the chroman-4-one scaffold (encompassing atoms O2–C7–C8–C9–C10–C11–C12–C13–C14–C15) along with its associated substituents: a carbonyl oxygen (O3), a hydroxyl group (O4), a methoxy group (C17–O5), and a methyl group (C16). The second moiety is a hydroxyl-substituted phenyl ring (C1–C2–C3–C4–C5–C6 with hydroxyl O1). These two moieties are connected by a C4–C7 single bond, resulting in a specific spatial orientation. This is defined by the C3–C4–C7–O2 dihedral angle of 2.6° and the C3–C4–C7–C8 dihedral angle of 119.2°. Notably, the C7–C8 linkage within the chroman-4-one core is a single bond, not a double or triple bond, which in turn establishes specific bond angles such as C8–C7–O2 (109.9°), C4–C7–O2 (107.0°), and C4–C7–C8 (114.1°). Consequently, these structural features dictate a non-planar conformation for the molecule, which disrupts the extended π-conjugated system across the entire structure. An analysis of the crystal packing, performed using the PLATON and Mercury software packages,[19,20] reveals that the supramolecular structure is primarily stabilized by an extensive network of hydrogen bonds. The key interactions include O–H···O hydrogen bonds (O1–H1···O3$^{-x,\,-1/2+y,\,2-z}$, O4–H4···O3) and C–H···O hydrogen bonds (C3–H3···O2, C16–H16A···O2 and C17–H17B···O1$^{-x,\,1/2+y,\,1-z}$) (see the figure, part b and c). In contrast, π–π stacking interactions are notably absent. The shortest centroid-to-centroid distance between adjacent aromatic rings is 4.7651 Å, which is significantly larger than the typical range (3.3–4.0 Å) required for effective stacking. Therefore, it can be concluded that hydrogen bonding is the dominant force governing the crystal packing.

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