

5,3'-Dihydroxy-3,6,7,4'-tetramethoxyflavone

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Key indicators

Single-crystal X-ray study

T = 294 K

Mean $\sigma(C-C)$ = 0.004 Å

R factor = 0.094

wR factor = 0.215

Data-to-parameter ratio = 13.5

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

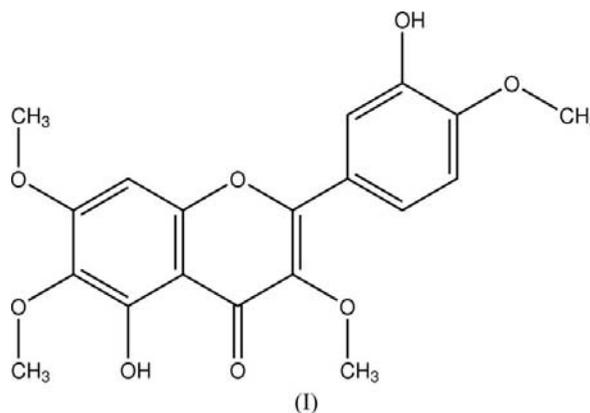
The title compound [systematic name: 5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-3,6,7-trimethoxychromen-4-one (casticin)], C₁₉H₁₈O₈, was isolated from the seeds of *Vitex agnus-castus* L. The fused chromene ring system and the benzene ring bonded to it are close to coplanar, with a dihedral angle between their respective mean planes of 8.30 (12)°. The two hydroxy H atoms are involved in intramolecular O—H···O hydrogen bonding. Intermolecular O—H···O and C—H···O hydrogen bonds and π – π interactions help to stabilize the crystal structure.

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Comment

Vitex agnus-castus L. (Verbenaceae), which has been used as a herbal medicine for centuries, is a shrub that grows widely in Mediterranean countries, central Asia and many other regions in the world (Doğan & Mert, 1998). Flavonoid extracts of the dried ripe berries (*Agni casti fructus*) of this species have been used in the treatment of many conditions, such as menstrual cycle disorders, premenstrual syndrome (PMS), menopause and disrupted lactation (Liu *et al.*, 2001; Mitwally *et al.*, 2002; Daniele *et al.*, 2005). In the flavonoid extracts of the seeds of this species, the title compound, (I), is found to be the major constituent. We report here its crystal structure, which was performed as part of our structure-identification procedures.



The bond lengths and angles of the flavone ring system in (I) (Fig. 1) are comparable to those of 5,3'-dihydroxy-3,7,4',5'-tetramethoxyflavone (Etti *et al.*, 2005) and 5-hydroxy-3,7,3',4',5',-pentamethoxyflavone (Dachriyanus *et al.*, 2004). As expected, rings A (C4a/C5–C8/C8a), B (O1/O2/C3/C4/C4a/C8a) and C (C1'–C6') are planar, the dihedral angles between them being $A/B = 2.37$ (4)°, $A/C = 9.49$ (3)° and $B/C = 7.20$ (4)°. As indicated by the torsion angles (Table 1), the methoxy groups at the C3 and C6 positions are twisted out of the planes of the rings to which they are attached due to steric

crowding, whereas the other two, at C4' and C7, are in the corresponding planes.

Strong O5—H5···O4 and less strong O3'—H3'···O4' intramolecular hydrogen bonds (Table 2) are observed in the crystal structure of (I). In addition, intermolecular O—H···O hydrogen bonds (including an intermolecular O3'—H3'···O5' bond; see Table 2 for symmetry code), C—H···O interactions and partial π – π stacking interactions stabilize the crystal structure. The fused chromene ring system of one molecule partially associates with the chromene ring system of a neighboring molecule on one side, and the benzene ring of a third molecule on the other side, along the *a*-axis direction (Fig. 2).

Experimental

Air-dried seeds (1.0 kg) of *Vitex agnus-castus* L., collected in September 2003 from the Ayvalık region in Turkey and identified by Professor Bayram Yıldız of Balıkesir University, were extracted successively (15 d each) with petroleum ether, hexane, and chloroform. The chloroform extract was evaporated *in vacuo* to give 4.0 g of a yellow gum-like substance. This was column chromatographed over a silica gel 60 (Merck, 60–200 mesh) column and eluted with a chloroform/methanol (99:1) solvent system. Fractions 4 and 5 out of 1–10 were combined, the solvents removed under vacuum, then washed with methanol, filtered and air-dried. The resulting yellow solid was crystallized from ethyl acetate to give 220 mg of the title compound [m.p. 460–461 K, literature m.p. 460 K (Raffauf *et al.*, 1981)]. Single crystals suitable for X-ray diffraction were grown by slow evaporation of a concentrated benzene/methanol (20:1) solution under ambient conditions. MS *m/z* 374.7 (M^+). IR (KBr) ν_{\max} : 3436 (OH), 1656 (C=O), 1607 (C=C), 1587, 1553, and 1515 cm^{-1} (aromatic); UV (nm, ϵ in parentheses) λ_{\max} (CHCl₃) 252 (5900), 273 (6100), 340 (6800); ¹H NMR (300 MHz, CDCl₃): δ 12.56 (1H, s, OH at C5), 8.02 (1H, s, OH at C3'), 7.70 (1H, d, *J* = 2.1 Hz, H2'), 7.65 (1H, dd, *J* = 8.5, 2.3 Hz, H-6'), 6.98 (1H, d, *J* = 8.8 Hz, H-5'), 6.55 (1H, s, H8), 3.98, 3.96, 3.91, 3.87 (12H, singlets 4 × OMe); ¹³C NMR (75 MHz, CDCl₃): δ 179.0 (C4), 158.85 (C7), 156.25 (C5), 152.66 (C8a), 152.42 (C2), 150.08 (C4'), 146.36 (C3'), 138.80 (C6), 132.17 (C4a), 123.09 (C1'), 121.04 (C5'), 115.29 (C2'), 111.05 (C8), 106.54 (C4a), 90.58 (C6'), 60.90 (OMe at C6), 60.20 (OMe at C3), 56.46 (OMe at C7), 56.05 (OMe at C4').

Crystal data

C ₁₉ H ₁₈ O ₈	<i>Z</i> = 8
<i>M_r</i> = 374.33	<i>D_x</i> = 1.457 Mg m ⁻³
Monoclinic, <i>C2/c</i>	Cu K α radiation
<i>a</i> = 15.5353 (5) Å	μ = 0.97 mm ⁻¹
<i>b</i> = 12.4493 (3) Å	<i>T</i> = 294 (2) K
<i>c</i> = 17.6655 (3) Å	Block, yellow
β = 92.424 (2)°	0.35 × 0.25 × 0.15 mm
<i>V</i> = 3413.51 (15) Å ³	

Data collection

Enraf–Nonius CAD-4 diffractometer	3350 independent reflections
ω scans	2259 reflections with <i>I</i> > 2 σ (<i>I</i>)
Absorption correction: ψ scan (North <i>et al.</i> , 1968)	<i>R</i> _{int} = 0.029
<i>T</i> _{min} = 0.727, <i>T</i> _{max} = 0.868	θ_{\max} = 74.3°
3463 measured reflections	3 standard reflections
	frequency: 120 min
	intensity decay: 1%

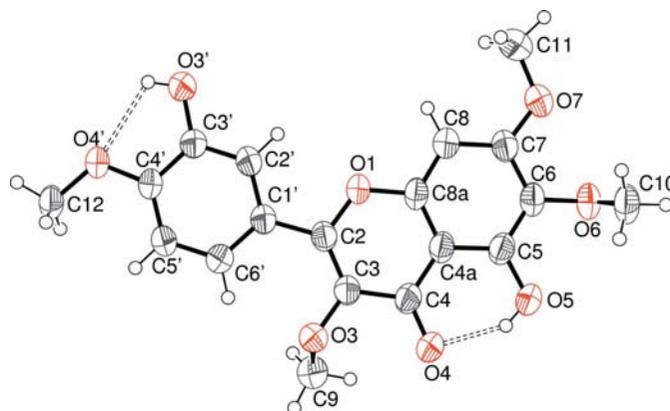


Figure 1

The structure of (I), with displacement ellipsoids drawn at the 50% probability level (arbitrary spheres for the H atoms) and hydrogen bonds indicated by dashed lines.

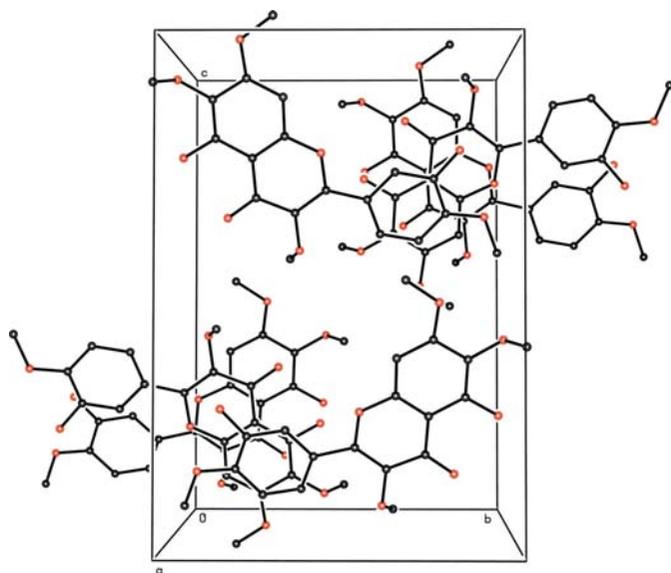


Figure 2

The packing of (I), viewed down the *a* axis, showing the overlap of aromatic ring systems. H atoms have been excluded for clarity.

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.094$
 $wR(F^2) = 0.216$
 $S = 1.10$
 3350 reflections
 248 parameters
 H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.1338P)^2 + 0.0496P]$$

$$\text{where } P = (F_o^2 + 2F_c^2)/3$$

$$(\Delta/\sigma)_{\max} < 0.001$$

$$\Delta\rho_{\max} = 0.98 \text{ e } \text{Å}^{-3}$$

$$\Delta\rho_{\min} = -0.71 \text{ e } \text{Å}^{-3}$$

Table 1

Selected torsion angles (°).

C9—O3—C3—C2	114.7 (3)	C10—O6—C6—C5	−88.3 (3)
C12—O4'—C4'—C5'	6.6 (4)	C11—O7—C7—C8	3.4 (5)

Table 2
Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O5—H5 \cdots O4	0.82	1.87	2.596 (3)	148
O3'—H3' \cdots O4'	0.82	2.24	2.687 (3)	115
O3'—H3' \cdots O5 ⁱ	0.82	2.15	2.935 (3)	161
O5—H5 \cdots O4 ⁱⁱⁱ	0.82	2.58	2.954 (3)	109
C10—H10b \cdots O7 ⁱⁱⁱ	0.96	2.54	3.491 (4)	173
C12—H12b \cdots O4 ⁱ	0.96	2.52	3.339 (4)	143

Symmetry codes: (i) $x, y - 1, z$; (ii) $x, y + 1, z$; (iii) $-x, -y + 2, -z$.

H atoms were positioned geometrically (O—H = 0.82 Å and C—H = 0.93–0.96 Å) and refined as riding, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{carrier})$ for aromatic H or $1.5U_{\text{eq}}(\text{carrier})$ for all other H atoms.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1993); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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