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Hydrogen bonding and π–π stacking in dimethylgenistein

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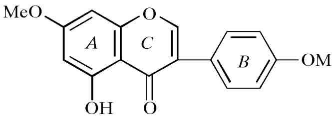
The title compound, 5-hydroxy-4′,7-dimethoxyisoflavone, $C_{17}H_{14}O_5$, is composed of a benzopyranone moiety, a phenyl moiety and two methoxy groups. The benzopyranone ring is not coplanar with the phenyl ring, the dihedral angle between them being 56.28 (3)°. The two methoxy groups are nearly coplanar with their corresponding rings, having C—C—O—C torsion angles of 2.9 (2) and 5.9 (2)°. The molecules are linked by C—H···O hydrogen bonds into sheets containing classical centrosymmetric $R_2^2(8)$ rings. The sheets are further linked by aromatic π–π stacking interactions and C—H···O hydrogen bonds into a supramolecular structure.

Comment

Hydrogen bonds and π–π stacking interactions are an important research area in supramolecular chemistry and crystal engineering (MacDonald & Whitesides, 1994). These interactions play an important role in self-assembly and recognition of aromatic compounds (Janiak, 2000; Hunter & Sanders, 1990) as auxiliary stabilizing short contacts (William *et al.*, 1999; Luque *et al.*, 2001; Kaafarani *et al.*, 2001). In biomacromolecular systems, stacking interactions and hydrogen bonds are important for the double-helical DNA structure (Hunter, 1993); they can direct the intercalation of drugs into DNA (Wang *et al.*, 1984) and they contribute to the stability of the tertiary structure of proteins (Burley & Petsko, 1985).



(I)

Genistein, a natural soy isoflavone, has potential phytoestrogen (Hua *et al.*, 2003; Warren, 2002) and antioxidant activities (Ian *et al.*, 1995). Studies have also found genistein effective in inhibiting cardiovascular disease (Hwang *et al.*, 2001), tyrosine kinases (Nevala *et al.*, 2002) and cancer cell growth (Yuan *et al.*, 2003; W. F. Chen *et al.*, 2003), and in accelerating the formation of bone cells (X. W. Chen *et al.*, 2003). The title compound, namely 5-hydroxy-4′,7-dimethoxyisoflavone, (I), is a derivative of genistein and has potential medical applications. We report here the crystal structure of (I).

The title compound is composed of a benzopyranone moiety, a phenyl moiety and two methoxy groups (Fig. 1). The geometry of the isoflavone skeleton of (I) is similar to that of its analogue dalspinin (Lakshmi, *et al.*, 1996) with respect to most of the bond distances and angles. The atoms of the benzopyranone moiety, composed of rings *A* (C1–C6) and *C* (O1/C1/C6–C9), are almost coplanar, the dihedral angle between the rings being 1.37 (8)°. To avoid steric conflicts, the two rigid ring systems, *viz*. benzene ring *B* (C10–C15) and the benzopyranone moiety, are rotated by 56.28 (3)° with respect to one another. The methoxy group at atom C3 is nearly coplanar with ring *A*, as indicated by the C16—O4—C3—C2 torsion angle [2.9 (2)°]; the methoxy group at atom C13 is also coplanar with the attached ring, the C17—O5—C13—C12 torsion angle being 5.9 (2)°.

Fig. 2 shows how a cyclic dimer is formed through a supramolecular synthon, $R_2^2(8)$. Methoxy atom O4 acts as a hydrogen-bond acceptor, *via* atom H4, to atom C4 of ring *A*. In this manner, a centrosymmetric $R_2^2(8)$ ring is formed. Hydroxy atoms O2 from the two molecules linked by the $R_2^2(8)$ ring act as hydrogen-bond acceptors, *via* atoms H14, to atoms C14 of rings *B* in adjacent molecules. The combination of the C14—H14···O2 interaction and the $R_2^2(8)$ supramolecular synthon generates a $(10\overline{1})$ sheet, which includes two *A*, two *B* and two *C* rings from four molecules, and these six rings are almost coplanar; furthermore, these dimers are also linked into (100) chains by C11—H11···O3 interactions (Fig. 3). The combination of the $(10\overline{1})$ sheets and the (100) chains generates a three-dimensional framework. An independent O2—H2O···O3 intramolecular hydrogen bonds generates a characteristic intramolecular *S*(6) motif. Details of the hydrogen bonding are given in Table 1.

Intermolecular stacking *via* aromatic π–π interactions is also present (Fig. 3), the two molecules being offset by partial overlap of rings *B* (π rich) and *C* (π deficient). Ring *B* of one

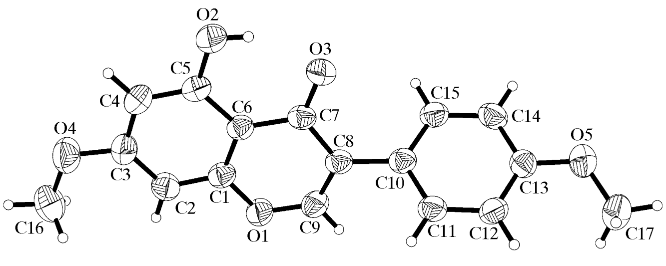


Figure 1
A view of the molecule of (I), showing the atom-numbering scheme and 50% probability displacement ellipsoids. H atoms are shown as spheres of arbitrary radii.

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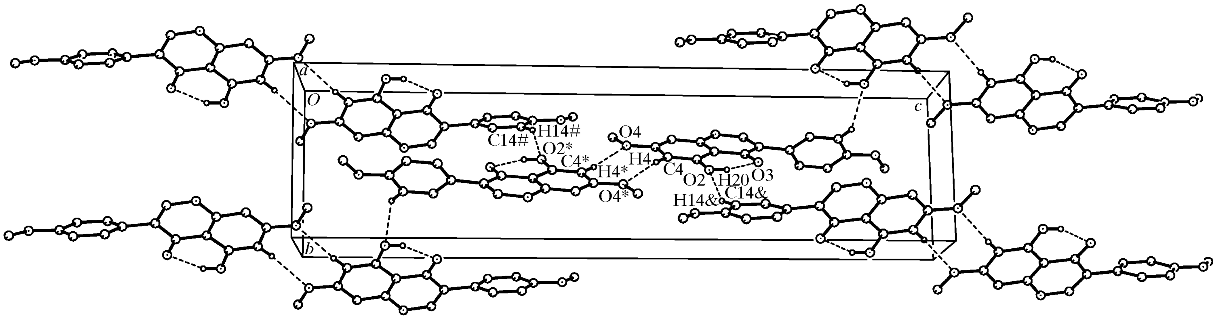

Figure 2
Part of the crystal structure of (I), showing the formation of the $(10\overline{1})$ sheets *via* hydrogen bonds. Atoms marked with an asterisk (*), hash (#) or ampersand (&) are at the symmetry positions $(1 - x, 1 - y, 1 - z)$, $(x - \frac{1}{2}, \frac{1}{2} - y, z - \frac{1}{2})$ and $(\frac{3}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z)$, respectively. For clarity, some H atoms have been omitted.

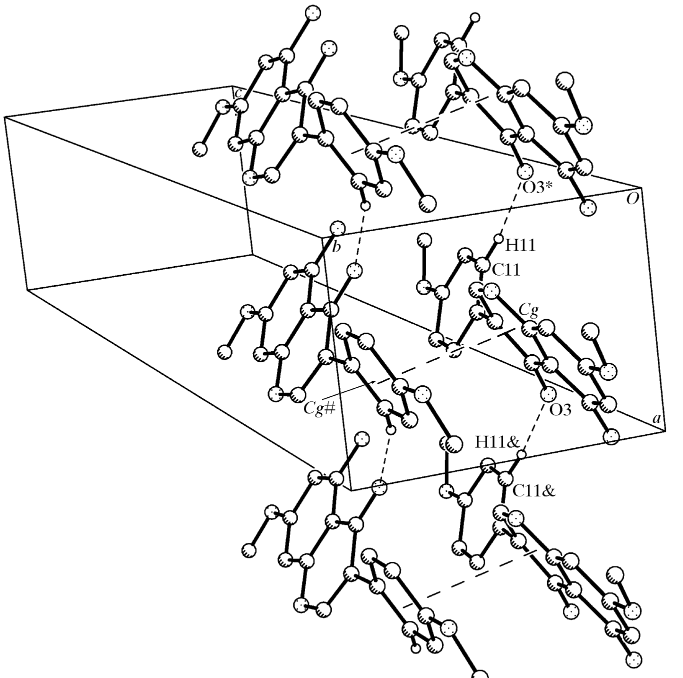

Figure 3
Part of the crystal structure of (I), showing the formation of the (100) chains *via* hydrogen bonds and π–π stacking interactions. Labels *Cg* represent the centroids of rings *A* and *C*. Atoms marked with an asterisk (*), hash (#) or ampersand (&) are at the symmetry positions $(1 - x, y, z)$, $(\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z)$ and $(1 + x, y, z)$, respectively. For clarity, some H atoms have been omitted.

molecule and ring *C* of a neighbouring molecule are almost parallel, with a dihedral angle between them of 8.02 (7)°. The perpendicular plane-to-plane distance between the rings is 3.311 Å, and the corresponding $Cg\cdots Cg\#$ distance is 3.693 Å [*Cg* represents the centroids of rings *A* and *C*; symmetry code: (#) $\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z$], indicating that a strong π–π stacking interaction exists in the title compound. Hydrogen bonds and aromatic π–π stacking interactions play a key role in assembling the supramolecular structure.

Experimental

Genistein (1.0 g) was dissolved in Na_2CO_3 (20 ml, 5%) and dimethyl sulfate (0.5 ml) was added dropwise to the solution with stirring. The mixture was stirred for 4 h at room temperature and a colourless precipitate began to appear. The precipitate was filtered off and washed with water until the pH of the filtrate was 8. After recrystallization from ethyl acetate, the product had a melting point of 428 K. Crystals of (I) suitable for X-ray analysis were obtained by slow evaporation from ethyl acetate after 7 d at room temperature.

Crystal data

$C_{17}H_{14}O_5$
$M_r = 298.28$
Monoclinic, $P2_1/n$
$a = 5.7754$ (8) Å
$b = 7.9446$ (12) Å
$c = 30.044$ (5) Å
$\beta = 93.807$ (12)°
$V = 1375.4$ (4) $Å^3$
$Z = 4$

$D_x = 1.441$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 34 reflections
$\theta = 2.7$–15.9°
$\mu = 0.11$ mm^{-1}
$T = 296$ (2) K
Prism, colourless
0.58 × 0.54 × 0.50 mm

Data collection

Siemens *P*4 diffractometer
ω scans
3089 measured reflections
2485 independent reflections
1673 reflections with $I > 2\sigma(I)$
$R_{int} = 0.010$
$\theta_{max} = 25.3$°

$h = -6 \rightarrow 6$
$k = 0 \rightarrow 9$
$l = -36 \rightarrow 36$
3 standard reflections every 97 reflections intensity decay: 0.4%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.035$
$wR(F^2) = 0.087$
$S = 0.90$
2485 reflections
203 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0522P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.19$ e $Å^{-3}$
$\Delta\rho_{min} = -0.15$ e $Å^{-3}$
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0233 (18)

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

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2O···O3	0.82	1.86	2.590 (2)	148
C4—H4···O4^{i}	0.93	2.54	3.459 (2)	171
C11—H11···O3^{ii}	0.93	2.56	3.464 (2)	164
C14—H14···O2^{iii}	0.93	2.58	3.399 (2)	147

Symmetry codes: (i) $1 - x, 1 - y, 1 - z$; (ii) $x - 1, y, z$; (iii) $\frac{3}{2} - x, y - \frac{1}{2}, \frac{3}{2} - z$.

H atoms were placed at calculated positions and treated as riding, with C—H distances in the range 0.93–0.96 Å and U_{iso}(H) values of $1.2U_{eq}$ of the attached C atom [$1.5U_{eq}$(C) for methyl H atoms].

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Siemens, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1473). Services for accessing these data are described at the back of the journal.

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