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Hexamethoxyamentoflavone trihydrate

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The molecular structure of the title compound [systematic name: 5,7,4′,5″,7″,4‴-hexamethoxy-3′,8″-biflavone trihydrate], $C_{36}H_{30}O_{10}\cdot3H_2O$, contains two flavone groups linked by a C—C single bond. In the crystal structure, centrosymmetric clusters are formed *via* intermolecular O—H⋯O hydrogen bonds involving the hexamethoxy-3′,8″-biflavone molecules and solvent water molecules.

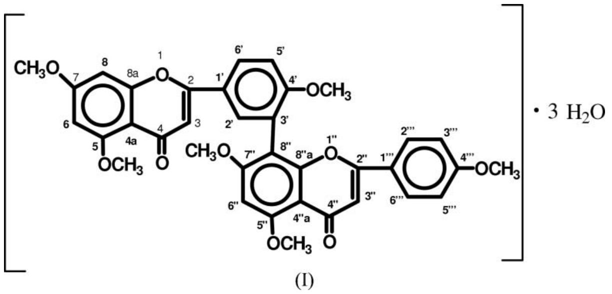
Key indicators

Single-crystal X-ray study
T = 299 K
Mean σ(C–C) = 0.012 Å
R factor = 0.087
wR factor = 0.269
Data-to-parameter ratio = 13.7

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

Comment

The species *Calophyllum* is indigenous to India and its varieties (*e.g. C. elatum*, *C. inophyllum*, *C. wighlankaensis*, *C. thwaitesis*, *C. walkeri*, *C. cordato oblongum*, *C. trapezifolium*, *C. calaba* and *C. bractealum*) are medicinal plants widely used as phytomedicines all over South Asia. All parts of *Calophyllum tomentosum* are used for traditional Indian medicine in Ayurved (Mehrotra *et al.*, 1986). *C. tomentosum* is credited with hepato-protective, anti-oxidant and anti-HIV activity and is found as a major constituent in many Ayurved preparations such as Punnaga (Mehrotra *et al.*, 1986). Previous phytochemical investigations of *C. tomentosum* leaves revealed the presence of triterpenoids, stereoids, xanthonoids, apetaloids and coumarins (Babu *et al.*, 1994; Banerji *et al.*, 1994). As part of a search for novel inhibitors of HIV reverse transcriptase, a methanol extract of *C. tomentosum* was isolated and converted to the hexamethoxy derivative. The results of the *in vitro* anti-HIV activity of some biflavonoids has previously been reported (Lin *et al.*, 1997).



(I)

There are several publications which deal with the isolation of Amentoflavone from different sources (Goh *et al.*, 1992; Ampofo *et al.*, 1986) and the structure elucidation of (I) has already been studied by spectroscopic methods (Chari *et al.*, 1997). Here we report the crystal structure of the hexamethoxy derivative of amentoflavone. In the molecular structure of (I), two flavone groups are linked through a C—C single bond (Fig. 1). In the crystal structure, centrosymmetric clusters are formed *via* intermolecular O—H⋯O hydrogen bonds (Table 1) involving the hexamethoxy-3′,8″-biflavone molecules and solvent water molecules (Fig. 2).

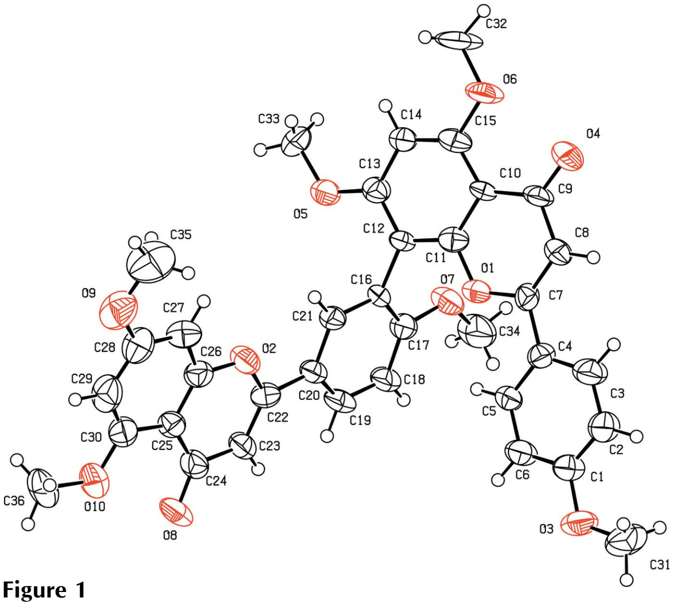


Figure 1
The molecular structure of (I), showing displacement ellipsoids drawn at the 30% probability level. The solvent water molecules have been omitted.

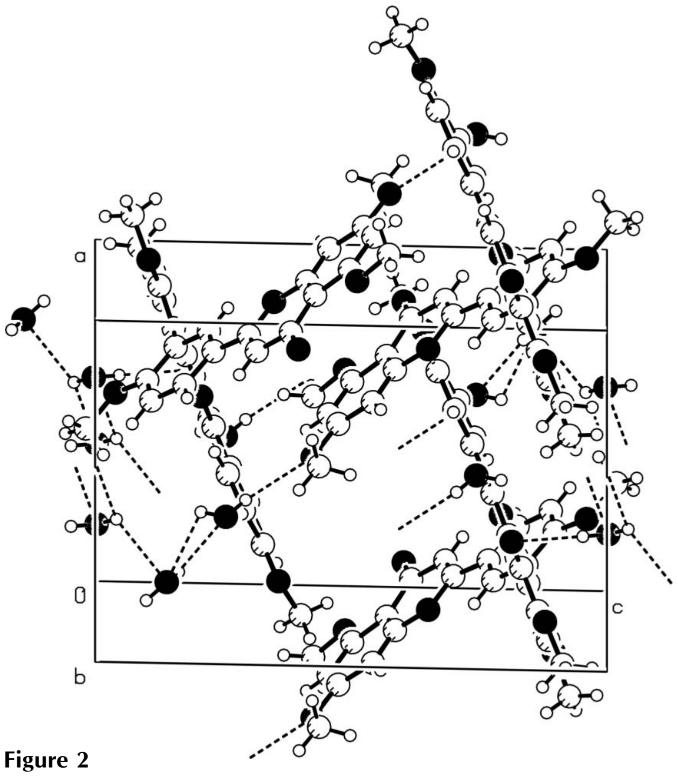


Figure 2
Part of the crystal structure of (I), showing hydrogen bonds as dashed lines.

Experimental

The title parent biflavone (amentoflavone) was isolated as a major constituent (0.2%) from a methanol extract of *C. tomentosum* by column chromatography over silica gel with gradient elution using a methanol and chloroform mixture as solvent system followed by purification with preparative thin-layer chromatography (PTLC). Attempts to crystallize the compound from different solvent systems were unsuccessful. In order to overcome this difficulty, it was methylated with diazomethane in diethyl ether as follows. For the methylation of amentoflavone, the parent compound (500 mg) was dissolved in methanol (15 ml) and cooled to 273–278 K and a freshly prepared ethereal solution of excess diazomethane was added dropwise. The solution was allowed to stand for 1 h at 273–278 K to complete the reaction. The solvents and excess diazomethane were removed by passing a stream of nitrogen gas to afford a pale-yellow amorphous solid. Among the spectroscopic analyses, ^{1}H NMR spectra of the product revealed the formation of a tetramethyl ether of amentoflavone. The remaining two chelated –OH groups were further methylated with CH_3I/Ag_2O in dry acetone to yield the hexamethyl ether. The crude reaction product was purified by PTLC followed by crystallization from hexane–ethyl acetate (4:1) (yield 90%). Crystals suitable for X-ray diffraction were obtained by recrystallization from hexane–ethyl acetate (4:1) at room temperature by slow evaporation. The water is probably incorporated during extraction of the material from plant leaves containing water.

Crystal data

$C_{36}H_{30}O_{10}\cdot 3H_2O$
M_r = 676.65
Triclinic, $P\overline{1}$
a = 10.275 (1) Å
b = 11.398 (1) Å
c = 15.068 (1) Å
α = 91.95 (1)°
β = 91.13 (1)°
γ = 102.40 (1)°
V = 1721.9 (3) Å^3
Z = 2
D_x = 1.305 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 0.84 mm^{-1}
T = 299 (2) K
Prism, yellow
0.20 × 0.10 × 0.03 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
7441 measured reflections
6128 independent reflections
1753 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.066
$\theta_{\rm max}$ = 66.9°
3 standard reflections
frequency: 120 min
intensity decay: 3.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.087
$wR(F^2)$ = 0.269
S = 0.93
6128 reflections
448 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0995P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max}$ = 0.008
$\Delta\rho_{\rm max}$ = 0.51 e Å^{-3}
$\Delta\rho_{\rm min}$ = −0.31 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O11—H111···O13	0.86	2.12	2.82 (2)	139
O11—H112···O11$^{\rm i}$	0.85	2.09	2.810 (19)	142
O12—H121···O9$^{\rm ii}$	0.85	2.53	3.061 (16)	122
O12—H122···O13	0.86	2.29	2.76 (2)	114

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

H atoms boned to C atoms were placed in calulated positions with C—H distances of 0.93 or 0.96 Å (methyl) and included in the refinement in riding approximation, with $U_{\rm iso}$(H) = $1.2U_{\rm eq}$(C) or $1.5U_{\rm eq}$(methyl C). The water H atoms were found in a difference map. They were refined with restrained geometry according to Nardelli (1999). The crystal diffracted very weakly and only 29% of the collected data are considered observed. The presence of the large anount of weak data has lowered the precision of the structure.

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Data collection: *CAD-4-PC Software* (Nonius, 1996); cell refinement: *CAD-4-PC Software*; data reduction: *REDU4* (Stoe & Cie, 1987); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

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