

A pimpinellin monomer and dimer isolated from the roots of *Esenbeckia grandiflora*

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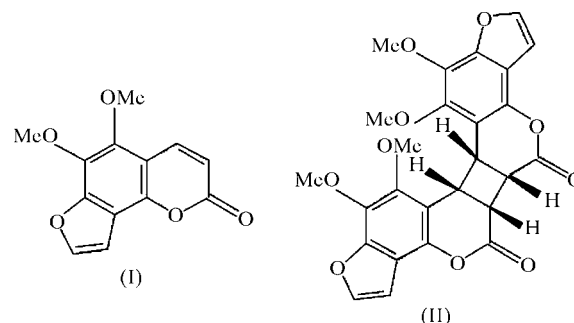
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X-ray diffraction studies carried out on single crystals of the monomeric, *viz.* 5,6-dimethoxy-2*H*-furo[2,3-*h*][1]benzopyran-2-one, C₁₃H₁₀O₅, and dimeric, *viz.* 5,5',6,6'-tetramethoxy-3,3',4,4'-tetrahydro-2*H*,2'*H*-3,3':4,4'-bi(furo[2,3-*h*][1]benzopyran)-2,2'-dione, C₂₆H₂₀O₁₀, forms of pimpinellin have revealed that, following cyclodimerization, the carbonyl groups are head-to-head with respect to one another. In the monomer, the heterocyclic ring is planar, but it exhibits a twisted-boat conformation in the dimer. Both the monomer and the dimer interact through C—H···O interactions.

Comment

Fur(an)ocoumarins have received much attention on account of their ability to perform cycloaddition reactions with DNA during irradiation with UV light (Zarbska, 1994; Moor & Gasparro, 1996; Brown, 2001), a property that has given rise to wide-ranging photochemotherapeutic applications (Miolo *et al.*, 1989). The furanocoumarins can also undergo cyclodimerization reactions, leading to the possibility of formation of different configurational isomers that may be of the head-to-head or head-to-tail type (Krauch *et al.*, 1966; Zdero *et al.*, 1990; Rojas-Lima *et al.*, 1999). A 1:2 mixture of the monomer, (I), and the dimer, (II), of the furanocoumarin pimpinellin was isolated, and the individual components were identified on the basis of their spectral data. The main indications of the presence of the dimeric molecule were the absence of the H and C atoms associated with the coumarin double bond present in the monomer [δ_{H} : 6.38 and 8.09 (*d*, *J* = 9.7 Hz); δ_{C} : 114.13 and 140.33], and the presence of signals for a carbonyl group (δ_{C} : 165.05), two saturated C atoms (δ_{C} : 40.21 and 38.64) and two methoxy groups (δ_{C} : 61.17 and 61.15). A combination of two-dimensional NMR experiments (¹H–¹H COSY, HMQC and HMBC) and comparison with data of models in the literature (Zdero *et al.*, 1990; Rojas-Lima *et al.*, 1999) supported all assignments of the ¹H and ¹³C chemical shifts. The stereochemistry of the pimpinellin dimer, however, could

not be deduced directly from the NMR data, and X-ray diffraction analysis was employed to establish its *cis*–*syn* conformation.



The structure of the monomer, (I), of pimpinellin is shown in Fig. 1. The atoms of the three rings of the molecule are nearly coplanar; the largest deviation [0.044 (2) Å] from the least-squares plane is exhibited by atom C1. An interesting feature of the packing of the structure is that the two methoxy groups, C12/O4 and C13/O5, exhibit a *syn* conformation, even though MM2 and AM1 calculations indicate that this conformer should be around 1.4 kcal mol^{−1} less stable than the *anti* conformer. It is suggested that the monomer of pimpinellin crystallizes as the *syn* conformer in order to facilitate the formation of two non-classical hydrogen bonds, *viz.* C12—H12C···O4ⁱ and C13—H13C···O3ⁱⁱ [symmetry codes: (i) 1 + *x*, *y*, *z*; (ii) $-\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z$], as shown in Fig. 2.

The asymmetric unit of the pimpinellin dimer, (II), was chosen so that it contained two independent molecules of

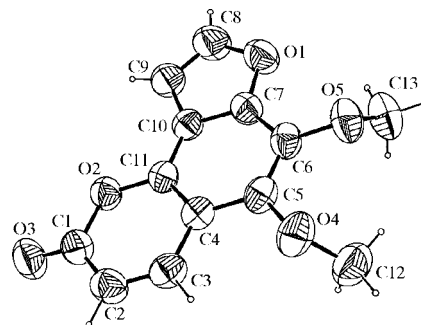


Figure 1
 An ellipsoid plot of the monomer (I), showing the atom labelling and 50% probability displacement ellipsoids.

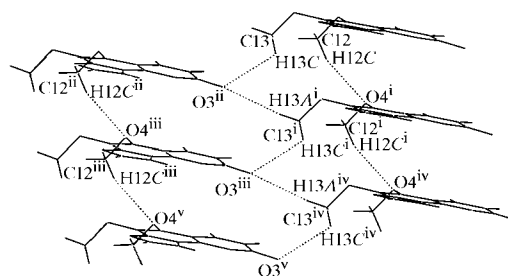


Figure 2
 A projection of the molecular packing of (I) along the *a* axis. [Symmetry codes: (i) 1 + *x*, *y*, *z*; (ii) $-\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z$; (iii) $\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z$; (iv) 2 + *x*, *y*, *z*; (v) $\frac{3}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z$.]

opposite chirality that are not related by symmetry (Fig. 3). In one molecule, the C102, C103, C202, C203 chirality is *SSRR*, while in the other molecule the C302, C303, C402, C403 chirality is *RRSS*. No significant conformational differences were observed between these independent molecules, however, and the bond lengths and angles are in good agreement (within experimental error) with literature values. For the purposes of simplification, therefore, only one independent molecule is considered in the following discussion. The atoms of the furan and aromatic rings on each side of the dimer are coplanar; the mean deviations with respect to the reference plane of the ring atoms are 0.023 and 0.014 Å. Atoms O14, O15, O24 and O25 of the methoxy groups also lie in the mean plane of the ring atoms, at distances of 0.035 (3), 0.054 (3), 0.002 (3) and 0.065 (2) Å, respectively, from that plane. However, atoms C112, C113, C212 and C213 of the methoxy groups of (II) are located on opposite sides of the reference plane of the rings, in accordance with the angular

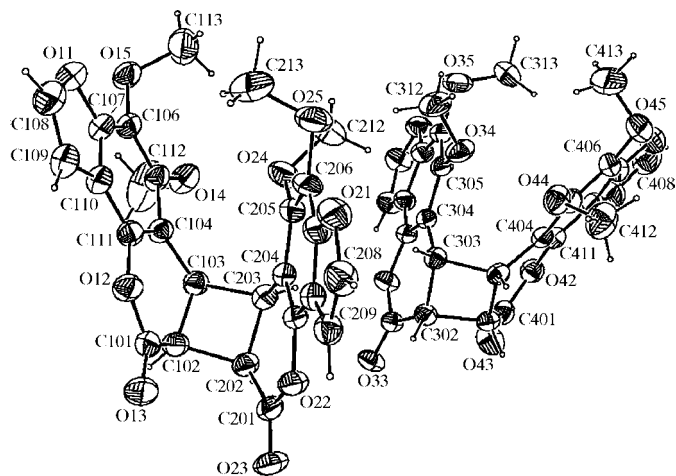


Figure 3
An ellipsoid plot of the dimer (II), showing the atom labelling and 30% probability displacement ellipsoids.

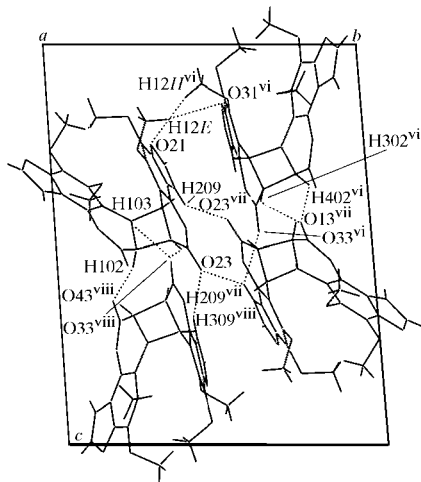


Figure 4
A projection of the molecular packing of (II) along the *a* axis. [Symmetry codes: (vi) $-1 + x, y, z$; (vii) $-1 - x, 1 - y, 1 - z$; (viii) $1 - x, 1 - y, 1 - z$.]

furanocoumarin nucleus. For these groups, the C104–C105–O14–C112, C105–C106–O15–C113, C207–C206–O25–C213 and C206–C205–O24–C212 torsion angles are 102.1 (4), -70.7 (6), -94.7 (5) and 49.1 (5)°, respectively. In the dimeric form of pimpinellin, the heterocyclic rings are in a twisted-boat conformation, as indicated by the Cremer & Pople (1975) puckering parameters (shown in Table 2 for both rings of the dimer). The distances of atoms O12, C101, C102 and C103 from the mean plane of the aromatic ring atoms are 0.034 (2), 0.198 (3), 0.277 (3) and 0.218 (3) Å, respectively. Atoms C102, C103, C202 and C203, which bind the monomer units to form the dimer, are in a twisted-square conformation, with a mean bond length of 1.562 Å. The four H atoms associated with these atoms are in *cis* positions, such that the pimpinellin dimer exhibits a *cis-syn* conformation. The dihedral angle between the least-squares planes passing through the furan and aromatic rings of the two monomers of the molecule is 38.3°. The molecules are held together by many weak secondary C–H···O interactions, as shown in Table 1. Fig. 4 depicts the molecular packing along the *a* axis. The *syn* stereochemistry of the four H atoms in the cyclobutane ring of the dimer of pimpinellin, a conformation also observed in the excited singlet state of coumarin (Hoffman *et al.*, 1971), suggests that (II) was formed when the pimpinellin monomer was photo-irradiated during the process of isolation. In the singlet-state photodimerization reaction of olefins, the set of orbitals involved in the reaction have identical energies. The very strong bonding interactions should lead to the formation of the *endo* head-to-head adduct, which is preferred over the *exo* head-to-head adduct by virtue of the secondary orbital interactions. The crystallographic study of the dimer of pimpinellin revealed that both carbonyl groups, O13 and O23, of the monomers are positioned on the same side of the molecule, characterizing the conformation as head-to-head. This finding is particularly significant in providing information concerning the mode of cyclodimerization of the pimpinellin monomers.

Experimental

A mixture of pimpinellin monomer and dimer was isolated from the C₆H₁₄ fraction from roots of *Esenbeckia grandiflora*. Crystals were grown at room temperature from a CHCl₃ solution in liquid diffusion with C₆H₁₄ for the monomer, and by slow evaporation from a CHCl₃ solution for the dimer.

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

D–H···A	D–H	H···A	D···A	D–H···A
C103–H103···O33 ^{viii}	0.98	2.55	3.320 (4)	135
C202–H202···O33 ^{viii}	0.98	2.59	3.353 (5)	135
C212–H12E···O31 ^{vi}	0.96	2.54	3.477 (5)	166
C209–H209···O23 ^{vii}	0.93	2.60	3.378 (4)	142
C209–H209···O33 ^{ix}	0.93	2.57	3.297 (4)	136
C309–H309···O23 ^{viii}	0.93	2.35	3.244 (5)	161
C302–H302···O13 ^{ix}	0.98	2.57	3.272 (4)	129
C312–H12H···O21 ⁱ	0.96	2.56	3.499 (5)	165
C402–H402···O13 ^{ix}	0.98	2.46	3.196 (4)	132

Symmetry codes: (i) $1 + x, y, z$; (vi) $-1 + x, y, z$; (vii) $-1 - x, 1 - y, 1 - z$; (viii) $1 - x, 1 - y, 1 - z$; (ix) $-x, 1 - y, 1 - z$.

Table 2
Cremer & Pople (1975) puckering parameters (\AA , $^\circ$) for (II).

Ring	q_2	q_3	φ_2	θ_2	Q
C101—O12—C111—C104—C103—C102	2.321 (3)	0.034 (3)	151.41 (8)	89.16 (8)	2.322 (3)
C201—O22—C211—C204—C203—C202	1.445 (3)	0.053 (3)	155.6 (1)	87.9 (1)	1.445 (3)

Compound (I)

Crystal data

$C_{13}H_{10}O_5$
 $M_r = 246.21$
 Monoclinic, $P2_1/n$
 $a = 3.90690$ (10) \AA
 $b = 13.4984$ (5) \AA
 $c = 20.9360$ (9) \AA
 $\beta = 91.733$ (2) $^\circ$
 $V = 1103.59$ (7) \AA^3
 $Z = 4$
 $D_x = 1.482$ Mg m $^{-3}$

Data collection

Nonius KappaCCD diffractometer
 φ scans
 4519 measured reflections
 2491 independent reflections
 1609 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.029$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.056$
 $wR(F^2) = 0.153$
 $S = 1.03$
 2491 reflections
 163 parameters
 H-atom parameters constrained

Mo $K\alpha$ radiation
 Cell parameters from 2383 reflections
 $\theta = 1.0$ – 27.5°
 $\mu = 0.12$ mm $^{-1}$
 $T = 293$ (2) K
 Irregular, colourless
 $0.30 \times 0.23 \times 0.20$ mm

$\theta_{max} = 27.5^\circ$
 $h = -5 \rightarrow 5$
 $k = -16 \rightarrow 17$
 $l = -27 \rightarrow 27$

$w = 1/[\sigma^2(F_o^2) + (0.0642P)^2 + 0.3P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} < 0.001$
 $\Delta\rho_{max} = 0.17$ e \AA^{-3}
 $\Delta\rho_{min} = -0.17$ e \AA^{-3}

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.076$
 $wR(F^2) = 0.183$
 $S = 1.01$
 10375 reflections
 650 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0545P)^2 + 0.6753P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.001$
 $\Delta\rho_{max} = 0.19$ e \AA^{-3}
 $\Delta\rho_{min} = -0.18$ e \AA^{-3}
 Extinction correction: *SHELXL97*
 Extinction coefficient: 0.0033 (10)

H atoms were positioned on stereochemical grounds and refined with fixed geometry, each riding on a carrier atom, with a $U_{iso}(H)$ value of 1.5 (for hydroxy H atoms) or 1.2 (for all other H atoms) times U_{eq} of the carrier atom.

For both compounds, data collection: *COLLECT* (Nonius, 1997–2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ1167). Services for accessing these data are described at the back of the journal.

Compound (II)

Crystal data

$C_{26}H_{20}O_{10}$
 $M_r = 492.44$
 Triclinic, $P\bar{1}$
 $a = 9.205$ (2) \AA
 $b = 14.285$ (4) \AA
 $c = 17.978$ (5) \AA
 $\alpha = 84.00$ (1) $^\circ$
 $\beta = 83.28$ (1) $^\circ$
 $\gamma = 77.66$ (1) $^\circ$
 $V = 2285.8$ (10) \AA^3

$Z = 4$
 $D_x = 1.431$ Mg m $^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 7179 reflections
 $\theta = 1.0$ – 27.5°
 $\mu = 0.11$ mm $^{-1}$
 $T = 293$ (2) K
 Irregular, colorless
 $0.30 \times 0.25 \times 0.20$ mm

Data collection

Nonius KappaCCD diffractometer
 φ scans
 15 850 measured reflections
 10 555 independent reflections
 4472 reflections with $I > 2\sigma(I)$

$R_{int} = 0.050$
 $\theta_{max} = 27.6^\circ$
 $h = -11 \rightarrow 11$
 $k = -18 \rightarrow 18$
 $l = -23 \rightarrow 20$

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