

## 7-Hydroxy-6-methoxy-3-[(2-oxo-2H-1-benzopyran-7-yl)oxy]-2H-1-benzopyran-2-one

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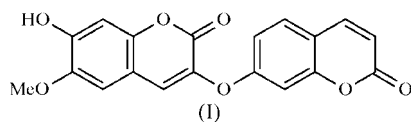
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The title compound, daphnoretin, C<sub>19</sub>H<sub>12</sub>O<sub>7</sub>, was isolated from the leaves of *Stellera chamaejasme* L. Two independent molecules are present in the asymmetric unit, with similar conformations. Each of the independent molecules is composed of two chromene systems connected by an ether bridge. The dihedral angles between the mean planes of the two chromene systems are 86.9 (2) and 81.9 (3)°. Molecules form chains *via* hydrogen bonds and adjacent chains are parallel to each other.

## Comment

*Stellera chamaejasme*, which is widespread in northern China, has been used traditionally as a herbal remedy for scabies and tinea. It has been found to possess obvious antitumor and antiviral, especially anti-HIV, activities (Ikekawa & Ikekawa, 1996; Endo *et al.*, 1998). *S. chamaejasme* contains large amounts of daphnoretin, (I), which has been demonstrated to inhibit Ehrlich carcinoma growth significantly (Hall *et al.*, 1982; Liou *et al.*, 1982) and has anti-P-388 lymphocytic leukemia activity *in vitro* (Handa *et al.*, 1983). It is also a protein kinase C activator, which shows strong suppressive effects on the expression of the hepatitis B surface antigen in human hepatoma Hep3B cells (Chen *et al.*, 1996) and induces



rabbit platelet aggregation through protein kinase C activation (Ko *et al.*, 1993). Antimicrobial effects are the other important characteristic of daphnoretin. It has antibacterial activity (Cottiglia *et al.*, 2001), and antifungal, antimitotic and anti-HIV-1 activities to some extent (Hu *et al.*, 2000). In our investigation of the chemical constituents of the leaves of *S.*

*chamaejasme*, (I) was isolated by chromatography and identified by X-ray diffraction. To the best of our knowledge, the crystal structure of (I) has not been reported previously.

Single-crystal X-ray diffraction reveals that two independent molecules of (I), *viz.* *A* and *B*, are present in the asymmetric unit, with similar conformations (Fig. 1). Each of the independent molecules contains two chromene systems, which are connected by an ether bridge. No significant difference is observed for bond distances and angles between molecules *A* and *B*, but they are distinguished by some bond rotations (Table 1). Rotations about the O1<sub>*n*</sub>–C1<sub>*n*</sub> and C1<sub>*n*</sub>–C10<sub>*n*</sub> bonds (*n* = *A* and *B*) mainly contribute to the different orientations of the chromene systems in the independent molecules. The atoms in each chromene system are nearly coplanar. The dihedral angles between the planes of the chromene ring systems are 81.9 (3) and 86.9 (2)° for molecules *A* and *B*. The conformations are also different at the terminal methoxy groups; the C19<sub>*n*</sub>–O7<sub>*n*</sub>–C14<sub>*n*</sub>–C13<sub>*n*</sub> torsion angles are 18.7 (3) and –1.5 (3)° for molecules *A* and *B*, respectively.

The bond distances and angles are in agreement with those of some analogous structures (Borowiak & Wolska, 1989; Rajnikant *et al.*, 1993; Gupta *et al.*, 1993; Singh *et al.*, 1995). The double bonds (C7<sub>*n*</sub>=O3<sub>*n*</sub> and C18<sub>*n*</sub>=O4<sub>*n*</sub>) and the multiple-character bonds (C5<sub>*n*</sub>=C6<sub>*n*</sub> and C10<sub>*n*</sub>=C11<sub>*n*</sub>), which are generally responsible for the photoactivity of coumarins (Song & Gordon, 1970), are confirmed by their respective distances [1.208 (2) and 1.212 (2) Å, 1.207 (2) and 1.210 (2) Å, 1.340 (2) and 1.343 (2) Å, and 1.333 (2) and 1.333 (2) Å for *A* and *B*, respectively]. The C8<sub>*n*</sub>–O2<sub>*n*</sub>, C7<sub>*n*</sub>–O2<sub>*n*</sub>, C17<sub>*n*</sub>–O5<sub>*n*</sub> and C18<sub>*n*</sub>–O5<sub>*n*</sub> bonds [1.3808 (19) and 1.3817 (19) Å, 1.372 (2) and 1.378 (2) Å, 1.381 (2) and 1.384 (2) Å, and 1.370 (2) and 1.371 (2) Å] exhibit variation in their distances, a feature quite common in furano compounds and simple coumarins [*e.g.* 1.389 and 1.366 Å in sphondin (Rajnikant *et al.*, 1993), and 1.390 and 1.368 Å in angenomalin (Gupta *et al.*, 1993)]. These differences may be due to ring strain and electron delocalization. The C–C–O and C–C–C angles at the junctions of the pyrone and benzene rings, *viz.*

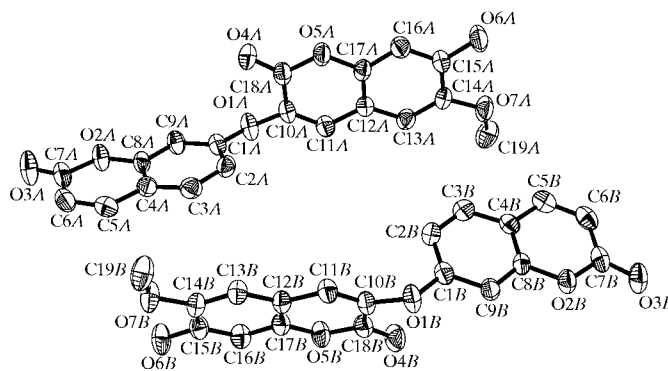
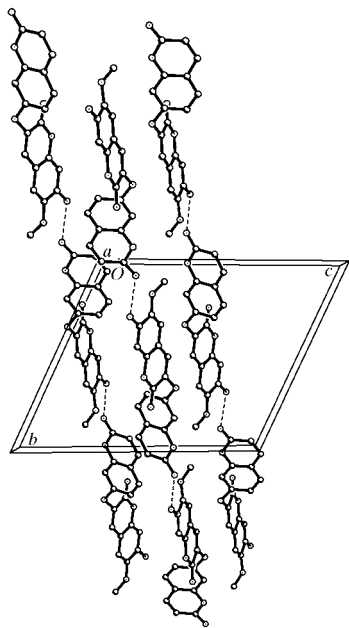


Figure 1

A view of the two independent molecules of the title compound, (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted.



**Figure 2**

A packing diagram for (I), viewed along the *a* axis, showing the one-dimensional chains formed *via* O—H...O interactions (dashed lines). H atoms have been omitted.

$C9n-C8n-O2n$  [ $116.48$  (17) and  $116.59$  (17) $^\circ$ ],  $C3n-C4n-C5n$  [ $125.40$  (19) and  $125.14$  (18) $^\circ$ ],  $C16n-C17n-O5n$  [ $117.22$  (16) and  $117.11$  (16) $^\circ$ ] and  $C11n-C12n-C13n$  [ $124.84$  (17) and  $124.54$  (17) $^\circ$ ], are slightly smaller than and slightly greater than  $120^\circ$ , respectively. This phenomenon has also been observed in some coumarin derivatives (Rajnikant *et al.*, 1993; Stemple & Watson, 1972; Ueno, 1985). The widening of the  $C6n-C7n-O3n$  [ $126.5$  (2) and  $127.1$  (2) $^\circ$ ] and  $C10n-C18n-O4n$  [ $126.23$  (18) and  $126.08$  (19) $^\circ$ ] angles is another feature commonly observed in 5-pyrone systems, and the large value of this angle is attributed to the lone-pair interactions between atoms  $O3n$  and  $O4n$  (Chinnakali *et al.*, 1999; Chinnakali & Sriraghavan, 1999; Singh *et al.*, 1997).

In the packing of (I) (Fig. 2), each molecule forms a one-dimensional chain *via* O—H...O hydrogen-bonding interactions between the O atoms of the hydroxy groups of benzene rings and ketone groups of pyrone rings (Table 2). Adjacent one-dimensional chains are parallel to each other.

## Experimental

The air-dried and crushed leaves of *S. chamaejasme* (2 kg) were extracted three times with 95% ethanol (36 l) for 30 min (for each extraction) by ultrasound-assisted leaching, and the extract after concentration was subsequently partitioned with petroleum ether and acetone. The acetone extract (86 g) was subjected to repeated column chromatography over silica gel, using petroleum ether–acetone mixtures of increasing polarity as eluants. The petroleum ether–acetone (7:3) fraction gave daphnoretin (52 mg). All purification steps were carried out at room temperature. Crystals grew from a mixed solution of ethanol and acetone (1:1). Daphnoretin was then recrystallized from  $CHCl_3$ –MeOH (1:1) as colorless blocks.

## Crystal data

$C_{19}H_{12}O_7$   
 $M_r = 352.29$   
 Triclinic,  $P\bar{1}$   
 $a = 7.659$  (3) Å  
 $b = 13.872$  (5) Å  
 $c = 16.479$  (5) Å  
 $\alpha = 113.175$  (5) $^\circ$   
 $\beta = 99.171$  (6) $^\circ$   
 $\gamma = 96.799$  (5) $^\circ$   
 $V = 1557.0$  (10) Å $^3$

$Z = 4$   
 $D_x = 1.503$  Mg m $^{-3}$   
 Mo  $K\alpha$  radiation  
 Cell parameters from 8396 reflections  
 $\theta = 1.4$ – $25.9^\circ$   
 $\mu = 0.12$  mm $^{-1}$   
 $T = 293$  (2) K  
 Block, colorless  
 $0.31 \times 0.16 \times 0.11$  mm

## Data collection

Rigaku R-Axis RAPID diffractometer  
 $\omega$  scans  
 Absorption correction: multi-scan (ABSCOR; Higashi, 1995)  
 $T_{min} = 0.966$ ,  $T_{max} = 0.985$   
 8458 measured reflections

5966 independent reflections  
 3894 reflections with  $I > 2\sigma(I)$   
 $R_{int} = 0.032$   
 $\theta_{max} = 26.0^\circ$   
 $h = -8 \rightarrow 9$   
 $k = -17 \rightarrow 17$   
 $l = -20 \rightarrow 19$

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.045$   
 $wR(F^2) = 0.093$   
 $S = 0.95$   
 5966 reflections  
 477 parameters

H-atom parameters constrained  
 $w = 1/[\sigma^2(F_o^2) + (0.0306P)^2]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} = 0.001$   
 $\Delta\rho_{max} = 0.17$  e Å $^{-3}$   
 $\Delta\rho_{min} = -0.17$  e Å $^{-3}$

**Table 1**

Selected torsion angles ( $^\circ$ ).

$C18A-C10A-O1A-C1A$	$-63.6$ (2)	$C18B-C10B-O1B-C1B$	$60.5$ (2)
$C2A-C1A-O1A-C10A$	$-29.3$ (3)	$C2B-C1B-O1B-C10B$	$38.9$ (2)
$C13A-C14A-O7A-C19A$	$18.7$ (3)	$C13B-C14B-O7B-C19B$	$-1.5$ (3)

**Table 2**

Hydrogen-bond geometry (Å,  $^\circ$ ).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$O6A-H6OA\cdots O3B^i$	$0.88$ (2)	$1.93$ (2)	$2.750$ (2)	$153$ (2)
$O6B-H6OB\cdots O3A^{ii}$	$0.87$ (2)	$1.95$ (2)	$2.776$ (2)	$157$ (2)

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

Atoms  $H6OA$  and  $H6OB$  were refined isotropically, with the O—H distances restrained to  $0.88$  Å. All other H atoms were placed in geometrically idealized positions and refined as riding atoms, with C—H distances of  $0.93$  (chromene) and  $0.96$  Å (methyl), and  $U_{iso}(H)$  values of  $1.2$  (chromene) or  $1.5$  (methyl) times  $U_{eq}(C)$ .

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *PROCESS-AUTO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus* (Sheldrick, 1990); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GZ1026). Services for accessing these data are described at the back of the journal.

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