Bull. Mater. Sci., Vol. 28, No. 7, December 2005, pp. 725–729. © Indian Academy of Sciences.

Supramolecular structure of S-(+)-marmesin—a linear dihydrofuranocoumarin

SANJEEV GOSWAMI, VIVEK K GUPTA*, ASHOK SHARMA† and B D GUPTA†

Post-Graduate Department of Physics, University of Jammu, Jammu Tawi 180 006, India
†Natural Products Chemistry Division, Regional Research Laboratory, Jammu Tawi 180 001, India

MS received 10 June 2005

Abstract. The title compound, $C_{14}H_{14}O_4$, a linear dihydrofuranocoumarin, was isolated from the bark of *Aegle marmelos*, a plant widely used in Ayurvedic system of medicine for the treatment of various ailments. The crystal structure was determined from X-ray diffraction data using direct methods. The compound crystallizes into monoclinic space group $P2_1$ with unit cell parameters: a = 5·721(1) Å, b = 13·810(1) Å, c = 7·864(2) Å, b = 100·39(1)°, Z = 2. The structure was refined by full-matrix least-squares to a final R value of 0·0523 for 1184 observed reflections. The benzopyran moiety is perfectly planar. The dihedral angle between the pyrone and benzene rings is 0·3(1)°. The furan ring has a 2a-envelope conformation. The molecules are linked by O–H…O hydrogen bonds into chains and these chains are linked into sheets by C–H…O hydrogen bonds. Further, the p–p stacking and C–H…p (arene) interactions link all of the sheets into a supramolecular structure.

Keywords. Supramolecular structure; direct methods; hydrogen bond; p–p interaction; envelope; furanocoumarin.

1. Introduction

Furanocoumarins are found to possess dermal photosensitizing activity (Musajo and Rodighiero 1962). The discovery of this unique activity of the furanocoumarins coupled with their utility in the treatment of leucoderma stimulated much activity among researchers seeking to evaluate other naturally occurring furanocoumarins as well as related synthetic compounds for the structure-activity profile of this interesting chemical nucleus. Furanocoumarins have received much attention on account of their ability to perform cycloaddition reactions with DNA during irradiation with UV light (Zarbska 1994; Moor and Gasparro 1996; Brown 2001), a property that has given rise to wide-ranging photochemotherapeutic applications (Miolo *et al* 1989). These coumarins have also found their way in the treatment of human immunodeficiency disease (North *et al* 1993). Therefore, these compounds are widely used in the field of medicine, and extensive future research into furanocoumarin derivatives is likely. The present study of the title compound is a part of our program to find the role of non-covalent intermolecular interactions in controlling the crystal packing of aromatic oxygen heterocycles. The understanding and utilization of all non-covalent interactions is of fundamental importance for further development of supramolecular chemistry and prediction of crystal structures.

2. Experimental

S-(+)-marmesin, [2,3-dihydro-2-(1-hydroxy-1-methylethyl)-7H-furo[3,2-g][1]benzopyran-7-one], was isolated first by Chatterjee and Mitra (1949) from the bark of *Aegle marmelos*, a plant commonly known in India as *Bael* and found wild all over the sub-Himalayan forests. The plant is widely used in Ayurvedic system of medicine for the treatment of various ailments. The bark of the plant has been reported to be used as a remedy in melancholia, intermittent fevers and palpitation of heart (Chopra *et al* 1956). Marmesin has also been isolated from *Ammi majus*, a plant used for the treatment of leucoderma (Abumustafa *et al* 1958). For the present study marmesin was isolated from the stem bark of *Aegle marmelos*. Dried and powdered stem bark (1 kg) of *Aegle marmelos* was extracted with methanol at room temperature and the concentrated extract (55 g) was chromatographed over a column of silica gel. Elution with ethyl acetate gave S-(+)-marmesin, m.p. 189–190°C. The chemical structure was assigned on the basis of ^{1}H NMR and mass spectral data (figure 1).

Transparent rectangular shaped single crystals of the title compound were grown at room temperature from

*Author for correspondence (vivek_gupta2k5@yahoo.co.in)

CCDC-250695 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

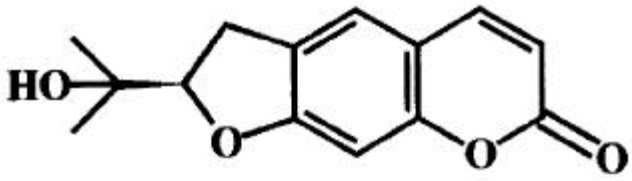

Figure 1. Chemical structure of S-(+)-marmesin.

Table 1. Crystal data and other experimental details.

CCDC number	250695
Crystal description	Transparent rectangular
Chemical formula	$C_{14}H_{14}O_4$
Molecular mass	246·25
Temperature	293(2) K
Unit cell dimensions	a = 5·721(1) Å, b = 13·810(1) Å, c = 7·864(1) Å, b = 100·39(1)°
Unit cell volume	611·1(1) Å^3
Z, calculated density	2, 1·338 Mgm^{-3}
Crystal system, space group	Monoclinic, $P2_1$
F(000)	260
Radiation/wavelength	CuKa/1·5418 Å
q range for entire data collection	5·72 < q < 69·9°
Reflections collected/unique	1200/1199 [R (int) = 0·0000]
Observed reflections with $I > 2\ s$ (I)	1184
No. of parameters refined	219
Refinement method	Full-matrix least-squares on F^2
Goodness-of-fit on F^2	1·080
Final R indices [$I > 2s$ (I)]	$R1$ = 0·0523, $wR2$ = 0·1637
R indices (all data)	$R1$ = 0·0526, $wR2$ = 0·1646
$(\Delta/s)_{max}$ in the final cycle	– 0·030 (for y H151)
Largest diff. peak and hole	0·246 and – 0·233 eÅ^{-3}

acetone–petroleum ether (1 : 1) by slow evaporation technique. Three-dimensional X-ray intensity data were collected on an Enraf Nonius CAD-4 diffractometer with CuKa radiation (l = 1·5418 Å) using a crystal of dimensions 0·4 × 0·2 × 0·2 mm. The unit cell dimensions were determined from an angular setting of 25 reflections. The intensity data of 1200 reflections were measured, using the w–2q scan technique (– 6 ≤ h ≤ 6, 0 ≤ k ≤ 16, 0 ≤ l ≤ 9). Three standard reflections (0 –2 2, 0 –3 2, 1 –2 2) measured every hour showed no significant variations. The space group was determined to be $P2_1$ from the systematic absences 0k0: k = 2n + 1. Data were corrected for Lorentz and polarization factors but no absorption correction was made.

The structure was solved by direct methods using SHELXS97 software (Sheldrick 1997). All non-hydrogen atoms of the molecule were obtained from the E-map. Full-matrix least-squares refinement was carried out using SHELXL97 software (Sheldrick 1997). All the hydrogen atoms were located on a difference electron density map and their positional and isotropic thermal parameters

Table 2. Atomic coordinates and equivalent isotropic thermal parameters (Å^2) for non-hydrogen atoms (e.s.d.'s are given in parenthesis).

Atom	x	y	z	U_{eq}*
O1	0·9761(4)	0·5874(2)	– 0·1818(3)	0·054(1)
C2	1·0608(5)	0·5612(3)	– 0·3423(4)	0·046(1)
C3	0·8749(6)	0·4927(3)	– 0·4405(4)	0·049(1)
C4	0·5723(5)	0·3914(2)	– 0·2972(4)	0·042(1)
C5	0·2932(6)	0·3108(2)	– 0·1321(4)	0·047(1)
C6	0·1990(6)	0·3052(3)	0·0124(5)	0·051(1)
C7	0·2792(5)	0·3687(2)	0·1569(4)	0·047(1)
O7	0·2125(5)	0·3676(2)	0·2948(3)	0·061(1)
O8	0·4470(4)	0·4367(2)	0·1379(3)	0·051(1)
C9	0·7130(6)	5·0157(3)	– 0·0104(4)	0·049(1)
C10	0·8096(5)	0·5220(2)	– 0·1592(4)	0·042(1)
C11	0·7417(5)	0·4612(2)	– 0·3022(4)	0·042(1)
C12	0·4703(5)	0·3809(2)	– 0·1479(4)	0·039(1)
C13	0·5435(5)	0·4433(2)	– 0·0095(4)	0·040(1)
C14	1·1077(5)	0·6541(2)	– 0·4345(3)	0·041(1)
C15	1·2008(7)	0·6276(3)	– 0·5990(5)	0·059(1)
C16	1·2853(6)	0·7172(3)	– 0·3178(5)	0·057(1)
O17	0·8886(4)	0·7038(2)	– 0·4899(3)	0·054(1)

*U_{eq} = (1/3) $\Sigma_i\Sigma_j U_{ij}\ a_i^*\ a_j^*\ a_i.a_j$

Table 3. Selected bond lengths (Å) and bond angles (°) for non hydrogen atoms (e.s.d.'s are given in parentheses).

C5–C6	1·345(4)	C5–C12	1·423(4)
C6–C7	1·443(5)	C7–O7	1·214(4)
C7–O8	1·370(4)	O8–C13	1·374(3)
C6–C7–O7	126·1(3)	O7–C7–O8	116·5(3)
C6–C7–O8	117·4(3)	C4–C12–C5	123·5(3)
O8–C13–C9	116·0(2)	–	–
O1–C2–C3–C11	– 17·4(3)	C2–C3–C11–C10	12·3(3)
C3–C11–C10–O1	– 2·2(4)	C11–C10–O1–C2	– 9·5(3)
C10–O1–C2–C3	17·1(3)	–	–

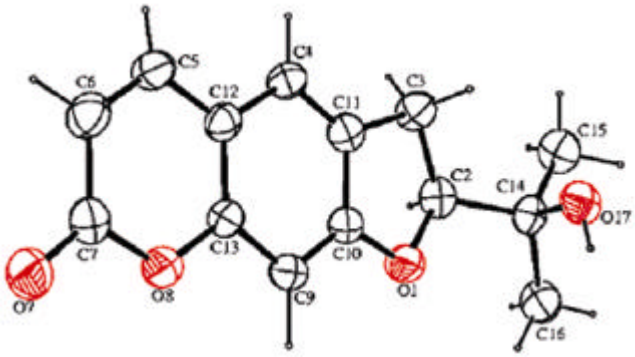

Figure 2. ORTEP view of the molecule with the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

were included in the refinement. The final refinement cycles converged were $R = 0{\cdot}0523$ and $wR(F^2) = 0{\cdot}1637$. The final weighting scheme was $w = 1/[s^2(F_0^2) + (0{\cdot}1552P)^2 + 0{\cdot}02P]$, where $P = [F_0^2 + 2F_c^2]/3$. Maximum shift to e.s.d. ratio for all atoms in the final cycle was – 0·030 (for *y*, H151). Atomic scattering factors were taken from International tables for X-ray Crystallography (1992, Vol. C, tables 4·2·6·8 and 6·1·1·4). The crystallographic data are summarized in table 1. CCDC-250695 contains the supplementary crystallographic data for this paper.

3. Results and discussion

The final atomic coordinates with equivalent isotropic displacement parameters are presented in table 2. Selected bond distances, bond angles and torsion angles are listed in table 3. An ORTEP view of the title compound with atomic labeling is shown in figure 2 (Farrugia 1997). The geometry of the molecule has been calculated using the software winGX (Farrugia 1999) and PARST (Nardelli 1983, 1995).

The bond distances and bond angles of the title compound are in good agreement with the corresponding values reported for related furanocoumarin derivatives (Stemple and Watson 1972; Gupta *et al* 1993; Singh *et al* 1995; Magotra *et al* 1995). In the benzopyran ring, the C6–C7 and C7–O8 distances are 1·443(5) Å and 1·370(4) Å, respectively, indicating that the electrons are delocalized

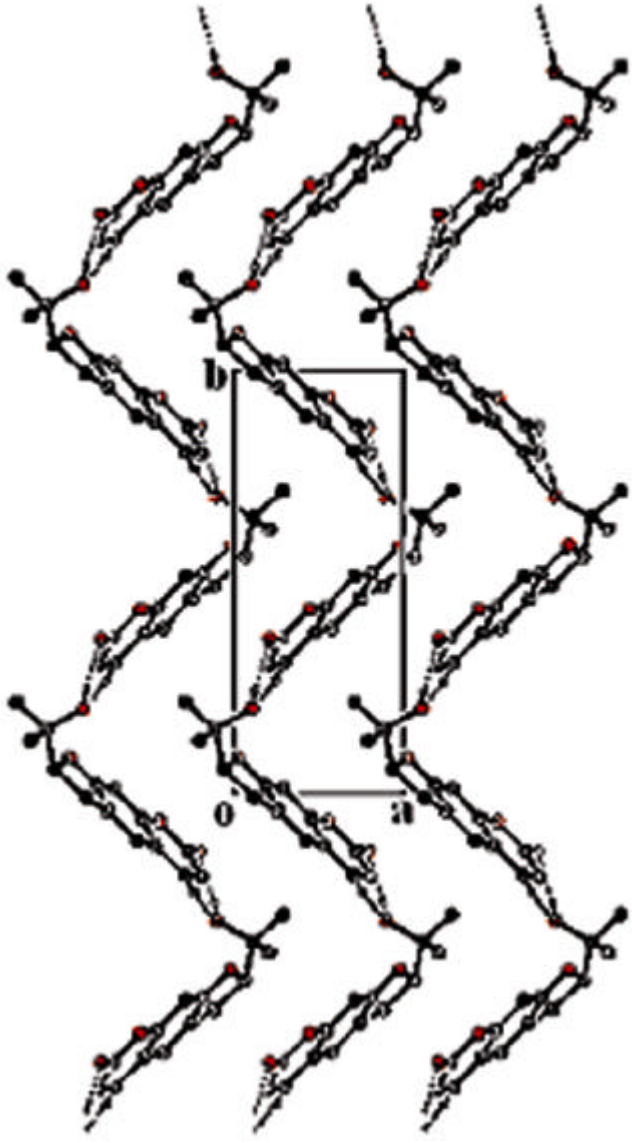

Figure 3. Part of the crystal structure showing the formation of O–H…O chains along *b*-axis.

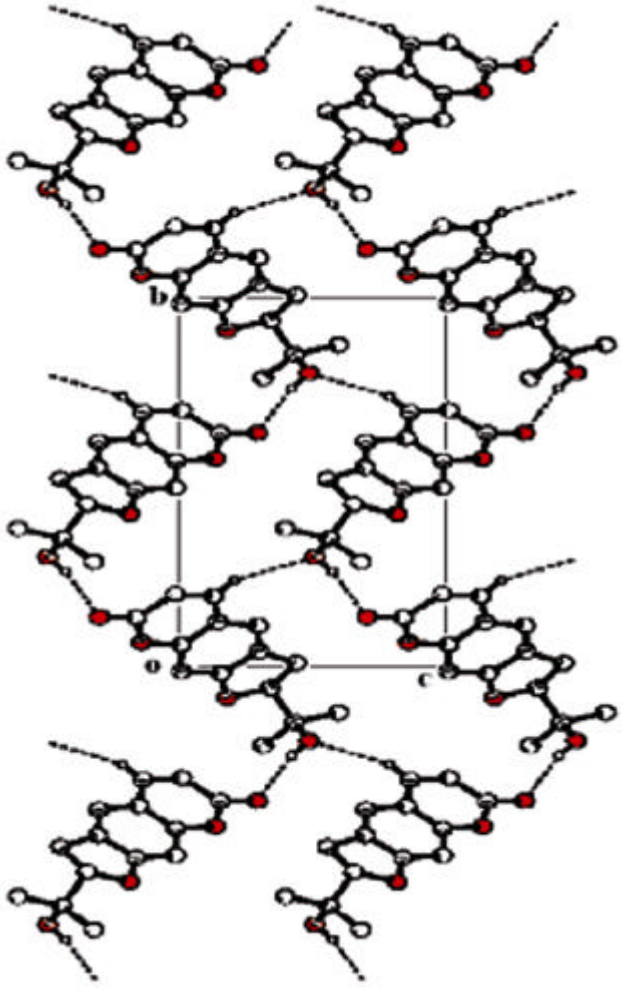

Figure 4. Part of the crystal structure down *a*-axis, showing the linking of chains into sheets by C–H…O hydrogen bond. For clarity, only H atoms involved in hydrogen bonding have been included.

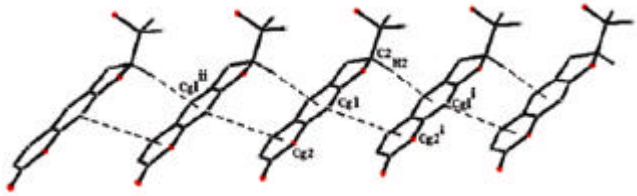

Figure 5. Molecular stacking along the *a*-axis showing the linking of the molecules by C–H…*p* and *p*–*p* interactions. Ring centroids involved in the C–H…*p* and *p*–*p* interactions are joined by dashed lines.

in the ring with the carbonyl group acting as the electron-withdrawing group. This is corroborated by the fact that the benzopyran ring is planar (maximum deviation, 0·014(4) Å for C6). The angles O8–C13–C9 and C4–C12–C5 at the junction of the pyrone and benzene rings are, respectively, smaller and greater than 120°. This causes the approach of O8 to C9 and the separation of C4 from C5. This feature found in coumarin derivatives is also present in the title compound. The widening of the angle O7–C7–O8 is another commonly occurring feature which is usually observed in coumarin systems and the large value of this angle is attributed to the lone-pair interactions between O7 and O8.

The furan ring has a 2*a*-envelope conformation with a phase angle of pseudorotation, $\Delta = 25{\cdot}47°$ and maximum angle of torsion, $f_m = 17{\cdot}84°$ (Altona *et al* 1968). The asymmetry parameter, $\Delta C_s(C2)$, which gives the distortion from ideal mirror symmetry bisecting the C10–C11 bond is 1·99 (Duax and Norton 1975). Atom C2 is disposed – 0·275(3) Å below the plane defined by the other four ring atoms. The dihedral angle between the planes of furan ring and benzopyran moiety is 3·8(1)°.

The supramolecular structure of marmesin is dictated by two intermolecular hydrogen bonds. The stronger of these two hydrogen bonds (O17–H17O…O7) gives rise to a chain running parallel to the [010] direction. Atom O17 of the hydroxy group in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor to carbonyl atom O7 in the molecule at (– *x* + 1, *y* + 1/2, – *z*), producing a chain (figure 3). The chains are linked into sheets by the second hydrogen bond (C5–H5…O17) (figure 4). Atom C5 in the molecule at (*x*, *y*, *z*) acts as a hydrogen bond donor to hydroxy atom O17 in the molecule at (– *x* + 1, *y* –1/2, – *z* + 1). There is one C–H...*p* (arene) hydrogen bond with H…centroid distance of less than 3·0 Å which serves to link all of the sheets into a single three-dimensional framework. Atom C2 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor to the benzene ring in the molecule at (*x* + 1, *y*, *z*). The three-dimensional framework of marmesin is further stabilized by *p*–*p* interactions between the pyrone and phenyl rings (figure 5). The interacting molecules are related by unit-cell translations along the short *a*-axis. Details of C–H…*p*, C–H…O, O–H…O hydrogen bonds, and *p*–*p* stacking interactions are given in tables 3 and 4, respectively.

4. Conclusions

(I) The dihedral angle between the pyrone and benzene rings is only 0·3(1)°, indicating the perfect planarity of the benzopyran moiety. The planarity of the benzopyran moiety confirms the aromatic character of this system.
(II) It is found in coumarin derivatives that the angles at the junction of the pyrone and benzene rings deviate significantly from 120°. This feature is also present in the title compound.
(III) An analysis of *p*–*p* interactions reveals that *p*–*p* stacking is an offset arrangement of the rings.
(IV) C–H…*p*, C–H…O, O–H…O hydrogen bonds, and *p*–*p* stacking interactions play a crucial part in assem-

Table 4. C–H…*p*, C–H…O and O–H…O hydrogen bonding geometry. Cg1 represents the centre of gravity of the phenyl ring.

D–H…A	D–H (Å)	D…A (Å)	H…A (Å)	D–H…A(°)
C2–H2…Cg1[i]	0·99(3)	3·703	2·721	169
C3–H32...O17	1·04(6)	2·944(5)	2·45(7)	108(4)
C5–H5...O17[iii]	0·86(6)	3·314(4)	2·51(5)	156(4)
O17–H17O...O7[iv]	0·78(6)	2·850(4)	2·09(6)	167(6)

Symmetry code: (i) $x + 1, y, z$; (iii) $-x + 1, y$-1/2, $-z + 1$; (iv) $-x + 1, y + 1/2, -z$

Table 5. Geometry of *p*–*p* interactions. Cg represents the centre of gravity of the following rings: Cg1 phenyl ring, Cg2 pyrone ring. CgI…CgJ represents the distance between the ring centroids; CgI…P, the perpendicular distance of the centroid of one ring from the plane of the other. *a* is the dihedral angle between the planes of rings I and J; *b* is the angle between normal to the centroid of ring I and the line joining ring centroids; Δ is the displacement of the centroid of ring J relative to the intersection point of the normal to the centroid of ring I and the least-squares plane of ring J.

CgI	CgJ	CgI…CgJ (Å)	CgI…P (Å)	*a* (°)	*b* (°)	Δ (Å)
1	2[i]	4·276	3·775	0·36	28·37	2·00
2	1[ii]	4·276	3·763	0·36	28·01	2·03

Symmetry code: (i) $x + 1, y, z$ and (ii) x-1, y, z

bling the molecules into an organized supramolecular structure.

Acknowledgements

The authors are grateful to Prof. T P Singh, Department of Biophysics, All India Institute of Medical Sciences, New Delhi, for providing the intensity data collection facility. (VKG) is grateful to the University Grants Commission, Govt. of India, for research funding under DRS Program [Project No. F-530/1/DRS/2001(SAP-I)].

References

Abumustafa E A, Badran N, Fayez M B E and Starkowsky N A 1958 *Nature* **154** 82

Altona C, Geise H J and Romers C 1968 *Tetrahedron* **24** 13

Brown D A 2001 *J. Photochem. Photobiol.* **B63** 148

Chatterjee A and Mitra S S 1949 *J. Am. Chem. Soc.* **71** 606

Chopra R N, Nayar S L and Chopra I C 1956 *Glossary of Indian medicinal plants* (New Delhi: CSIR) p. 8

Duax W and Norton D A 1975 *Atlas of steroid structures* (New York: Plenum) p. 1

Farrugia L J 1997 *J. Appl. Cryst.* **30** 565

Farrugia L J 1999 *J. Appl. Cryst.* **32** 837

Gupta V K, Rajnikant, Goswami K N, Mazumdar S K, Gupta B D and Banerjee S K 1993 *Cryst. Res. Technol.* **28** 187

Magotra D K, Gupta V K, Rajnikant, Goswami K N and Gupta B D 1995 *Acta Crystallogr.* **C51** 2637

Miolo G, Stefanids M, Santella R M, Dall'Acqua F and Gasparro F P 1989 *J. Photochem. Photobiol.* **B3** 102

Moor A C E and Gasparro F P 1996 *Clin. Dermatol.* **14** 353

Musajo L and Rodighiero G 1962 *Experientia* **18** 153

Nardelli M 1983 *Comput. Chem.* **7** 95

Nardelli M 1995 *J. Appl. Cryst.* **28** 659

North J, Neyndorff H and Levy J 1993 *J. Photochem. Photobiol.* **B17** 99

Sheldrick G M 1997 *SHELXS97 and SHELXL97* (Germany: University of Gottingen)

Singh A, Gupta V K, Rajnikant and Goswami K N 1995 *Mol. Mater.* **5** 289

Stemple N R and Watson W H 1972 *Acta Crystallogr.* **B28** 2485

Zarbska Z 1994 *J. Photochem. Photobiol.* **B23** 101