X-ray structure analysis of 3-chloro-7-hydroxy-4- methyl-chroman-2-one

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Abstract: The title compound crystallizes in the monoclinic space group P2$_1$/c, with unit cell parameters a= 7.7203(3), b=14.0481(4), c=8.9066(3) Å, =112.858(5)º, V= 890.11(5) Å^3 and Z = 4. The structure has been solved by direct methods and the final R-factor is 0.0433 for 2832 unique reflections. The molecule, as such, is planar and the planarity is confirmed by the magnitude of dihedral angles between the two rings. Extensive Hydrogen-bonding has been observed and chlorine atom is responsible for the formation of trifurcated hydrogen-bond. Trifurcated hydrogen-bond plays a significant role in the design and synthesis of molecules having drug implications.

Keywords: Coumarin, Crystal structure, Direct methods, Hydrogen bonding, X-ray crystallography

INTRODUCTION

Coumarins are naturally occurring benzopyrone derivatives. They occur in all plant parts from roots to flowers and fruits and are found widely spread in various plant families (Banerjee *et al.,* 1979). Coumarins have a wide variety of uses in perfume industry (Egan *et al.,* 1990) and also exhibit biological activities e.g., antithrombotic, vasodilating and photosensitizing effects, etc (Wolska, 1990). In view of some medicinal importance of coumarins and their possible applications(Rajnikant *et al*, 2004, 2005a, 2005b), we report the molecular and crystal structure of 3-chloro-7-hydroxy-4-methylchroman-2-one.

MATERIALS AND METHODS

The title compound in the powder form was purchased from Sigma-Aldrich (USA). It was first dissolved in chloroform and few drops of methanol were added later. The mixture was dissolved thoroughly in a sealed container kept at room temperature for slow evaporation. Good quality single crystals were obtained after a period of two weeks. The chemical structure of the title compound is shown in Fig. 1.

The activity of the molecule has been determined by making use of software (PASS). The information deduced from the computational process is the probability of a given molecule to be *active* (P$_a$) or *inactive* (P$_i$). This also gives us some indication about possible drug likeness which in the present case is 0.82 on a scale 0 to 1. Hence, from medicinal point of view, it becomes an important compound for three-dimensional single crystal X-ray studies.

A rectangular shaped single crystal of the title compound, having a well defined morphology (dimensions 0.30 mm x 0.20 mm x 0.15 mm) was used for three-dimensional crystal intensity data from X'Calibur computer- controlled single crystal X-ray diffractometer with CCD facility. Radiation used was MoK (=0.71073 Å). The intensities of various individual planes were recorded electronically with the help of a CCD camera. The cell measurement and refinement was carried at 293K (2). A total number of 5373 reflections were recorded in the range 3.2- 32.2° of which 2832 were found unique with index range -11<=h<=8,-20<=k<=20,-11<=l<=12. Using the cut-off criteria i.e., [Fo> 4 (Fo)], 2223 reflections were treated as observed. The data were collected by using CrysAlis^{Pro} (2007) and reduced by CrysAlis*RED* (2007) software. The structure of the title compound was obtained by employing direct methods using SHELXS86 (1986) software (Sheldrick, 1986). All non- hydrogen atoms of the molecule were located from the E-map (electron density map). Refinement was carried out by full-matrix least-squares method on F^2 using SHELXL97 (1997) software (Sheldrick, 1997). The anisotropic refinements with thermal parameters for non-hydrogen atoms and subsequent refinement cycles converged the R-factor to 0.0433. The maximum and minimum residual electron density is 0.431 and -0.227 e.Å^3, respectively.

RESULTS AND DISCUSSION

Table 1 contains all the important parameters related to experimental crystal data for the title compound. The atomic coordinates and equivalent isotropic displacement factors with e.s.d's for the non-hydrogen atoms are presented in Table 2. Bond distances and bond angles for all non-hydrogen atoms are listed in Table 3.

Table 1. Crystal data and structure refinement details.

Empirical formula	$C_{10}H_7ClO_3$
Formula weight	210.62
Temperature	293(2)K
Wavelength	0.71073Å
Crystal system, space group	Monoclinic, $P2_1/c$
Unit cell dimensions	a= 7.7203(3) Å, $= 90°$
	b= 14.0481(4) Å, $=112.858(5)°$
	c = 8.9066(3) Å, $= 90°$
Volume	890.11(5) Å^3
Z,Calculated density	4, 1.572 Mg/m^3
Absorption coefficient	0.402 mm-1
F(000)	432
Crystal size	0.30 mm x 0.20 mm x 0.15 mm
θ range for data collection	3.21 to 32.15°
Limiting indices	-11<=h<=8,-20<=k<=20,
	-11<=l<=12
Reflections collected/unique	5373/ 2832 [R(int) = 0.0145]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2832 / 0 / 156
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.1136
R indices (all data)	R1 = 0.0561, wR2 = 0.1194
Largest diff. peak and hole	0.431 and -0.227 e. Å^{-3}

Geometry of Intra and Intermolecular hydrogen bond interactions are presented in the Table 4. A general view of the molecule indicating atomic numbering scheme (thermal ellipsoids drawn at 50% probability level), is shown in Fig. 2 (Farrugia, 1997). Geometrical calculations have been performed using PARST program (Nardelli, 1995).

The molecule consist of two six-membered rings, a phenyl ring labeled as Ring A and to which is fused a pyrone ring, labeled as Ring B. The six C-C bond distances in the phenyl ring lie in the range 1.376(2)-1.405(2) Å (average value being 1.391(2) Å) which agrees

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å) with e.s.d.'s in parentheses, for the non-hydrogen atoms.

Atom	x	y	z	U(eq)*
Cl(1)	0.1163(1)	0.1252(1)	0.4804(1)	0.0047(1)
O(1)	-0.1244(1)	0.3558(1)	0.2386(1)	0.0033(1)
C(4)	-0.2811(2)	0.2239(1)	0.0658(2)	0.0029(1)
O(3)	0.1079(2)	0.3343(1)	0.4759(1)	0.0047(1)
C(5)	-0.2595(2)	0.3213(1)	0.0966(2)	0.0028(1)
C(3)	-0.1599(2)	0.1584(1)	0.1863(2)	0.0033(1)
C(2)	-0.0314(2)	0.1958(1)	0.3242(2)	0.0032(1)
C(8)	-0.5348(2)	0.2617(1)	-0.1913(2)	0.0039(1)
C(6)	-0.3684(2)	0.3892(1)	-0.0109(2)	0.0033(1)
O(2)	-0.6106(2)	0.4259(1)	-0.2627(2)	0.0052(1)
C(9)	-0.4235(2)	0.1958(1)	-0.0820(2)	0.0037(1)
C(1)	-0.0068(2)	0.2972(1)	-0.3557(2)	0.0032(1)
C(7)	-0.5064(2)	0.3587(1)	-0.1567(2)	0.0035(1)
C(10)	-0.1798(4)	0.0534(1)	0.1551(3)	0.0052(1)

$U_{eq}* = (1/3) “_i”_j U_{ij}a_i^*a_j^*(a_ia_j)$

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

Bond length (Å)			
Cl(1)-C(2)	1.728(1)	O(1)-C(1)	1.361(2)
O(1)-C(5)	1.378(1)	C(4)-C(5)	1.393(2)
O(3)-C(1)	1.211(2)	C(3)-C(10)	1.499(2)
Bond angles (°)			
C(1)-O(1)-C(5)	122.17(11)	C(9)-C(4)-C(3)	124.24(12)
O(1)-C(5)-C(6)	115.67(11)	C(2)-C(3)-C(4)	117.61(12)
C(2)-C(3)-C(10)	122.52(14)	C(4)-C(3)-C(10)	119.87(13)
C(3)-C(2)-C(1)	123.52(12)	C(3)-C(2)-Cl(1)	122.12(11)
C(1)-C(2)-Cl(1)	114.35(10)	O(3)-C(1)-O(1)	117.29(13)
O(3)-C(1)-C(2)	126.12(13)	O(1)-C(1)-C(2)	116.59(11)
O(2)-C(7)-C(6)	117.93(14)	O(2)-C(7)-C(8)	121.72(13)

reasonably well with the theoretical value (1.395(2) Å) quoted by Allen *et al.* (1987). The two C-O bonds, (O1-C1=1.361(2) Å; O1-C5= 1.378(1) Å), in the pyrone ring are in agreement with the C-O distances as obtained in some analogous structure of Rutaretin (Sharma, 2006). The double bond C1=O3 is confirmed by the distance 1.211(2) Å.

The bond angles, O1-C5-C6 [115.67(1)°] and C9-C4-C3[124.7(1)]°, at the junction of the pyrone and benzene rings are, respectively, smaller and greater than 120º. This phenomenon has also been observed in some analogous coumarins and this angular difference causes O1 to come closer to C6 and C3 to move away from C9 (Alock et al., 1972; Valente et al., 1975). The widening of the angle, O3-C1-C2=126.12(1)°, is attributed to lone-pair interactions between O1 and O3.   The C3-C10 (methyl) bond distance
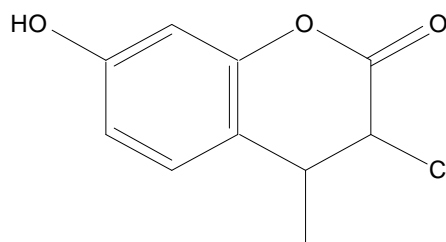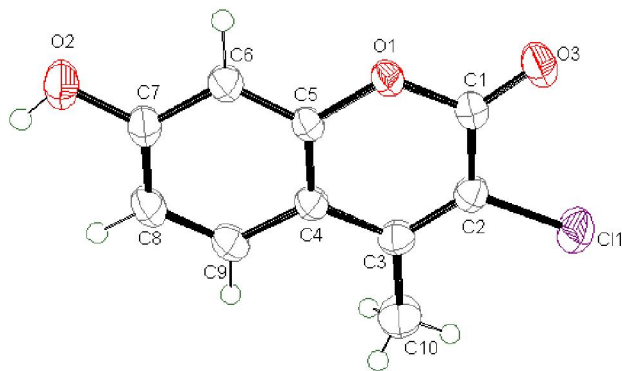

Fig. 1. *3-chloro-7hydroxy-4-methylchroman-2-one*

Fig. 2. *ORTEP view of the molecule (thermal ellipsoids drawn at 50% probability level).*

Table 4. Geometry of intra and intermolecular hydrogen bond interactions (e.s.d's in parentheses).

Atom	D-H	D...A	H...A	D-H....A
C10 -H10B ...Cl1 [(i)]	0.863(3)	3.081(2)	2.673(3)	110.29(2)
C6 -H6 ...Cl1[(ii)]	1.012(2)	3.801(2)	2.921(2)	145.88(1)
C6 -H6 ...O2[(iii)]	1.012(2)	3.608(2)	2.864(2)	130.84(1)
C8 -H8 ...O3[(iv)]	0.941(2)	3.329(2)	2.641(2)	130.38(1)
C8 -H8 ...Cl1[(iv)]	0.941(2)	3.655(1)	2.756(2)	160.08(1)
O2 -H12 ...O3[(iv)]	0.806(2)	2.805(2)	1.999(2)	177.39(2)
C10 -H10A...O3[(v)]	0.887(4)	3.412(2)	2.960(3)	113.50(2)
C10 -H10B...O1[(v)]	0.863(3)	3.520(2)	2.845(3)	136.31(2)
C10 -H10C ...O2[(vi)]	0.873(4)	3.684(3)	2.934(4)	145.11(3)

(i) x,y,z; (ii) -x,+y+1/2,-z+1/2; (iii) -x-1,-y+1,-z; (iv) x-1,+y,+z-1; (v) -x,+y-1/2,-z+1/2; (vi) x,-y+1/2,+z+1/2
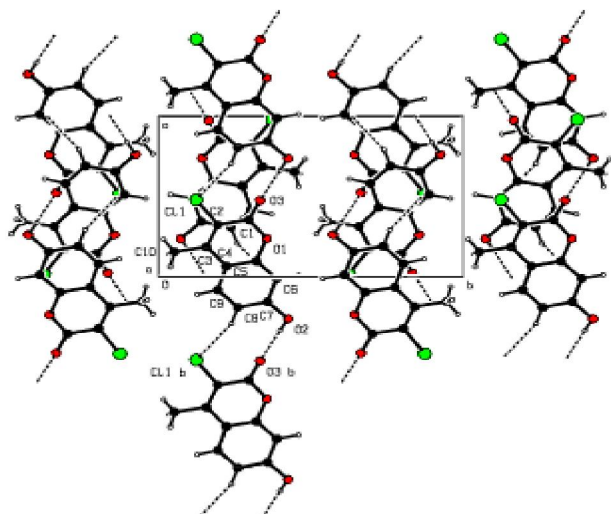
Fig. 3. *Hydrogen bonding network along a-axis.*

[1.499(2) Å] is strictly in agreement with the value obtained in case of 1H, 4H- tetrahydro-8-methyl-quinolizino-(9, 9a, 1g-h) Coumarin (Rajnikant *et al.*, 2004). The dihedral angle between the least-squares plane of Ring A and Ring B is 179.74(0.05) which is close to 180º. This means that the molecule is strictly planar and the individual rings do not exhibit any torsion along the ring-fusion bond (C5-C4).

The three-dimensional packing of molecules in the unit cell indicating hydrogen bonding along a-axis is shown in Fig. 3. The molecules along a-axis exhibits an overlap of pyrone ring of one molecule with the benzene ring of the neighbouring molecule. This results into the occurrence of some intermolecular interactions of the type C-H…O, O-H…O, C-H…Cl. The prominent among these are the C-H…Cl intermolecular interaction which gives rise to the bond geometry presented in Table 4 This gives rise to the formation of a trifurcated chloro-hydrogen bond. Such bonds play a significant role in the design and synthesis of molecules having drug implications. The molecules are stabilized in the unit cell by vander-Waal's forces.

Conclusions

The study concluded that the carbon-carbon bond distances in the phenyl ring have normal values. The molecule is strictly planar and the rings do not exhibit significant torsion along the ring-fusion bond. Molecular overlap as shown in the packing diagram results in the occurrence of intra- and intermolecular interactions. The presence of a trifurcated chloro-hydrogen bond is the most significant feature of structure analysis.

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