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Synthesis, ^{1}H NMR Study and Crystal determination of 7-Benzoyloxycoumarin

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ABSTRACT

The title compound, 7-benzoyloxycoumarin, $C_{16}H_{10}O_4$, crystallizes into monoclinic space group P2(1) with unit-cell parameter: a = 3.8479(7), b = 27.693(5), c = 5.7259(10) A^o. Z = 2. The crystal structure was solved by direct methods and refined to a final R-value of 0.0535 for 3295 observed reflection. The benzoyloxy ring present on 7- position was found to be almost coplanar with coumarin. The structure is stabilized by vander Waal's interactions. The structure of this compound was also established by ^{1}H NMR spectrum of its solution in $CDCl_3$.

Keywords: Synthesis, NMR, Crystal study, Coumarin, PCl_3.

INTRODUCTION

Many coumarins and its chemical analogous are expected for their anti-inflammatory, antiviral, antibacterial [1-3] and are being used clinically for curing platelet coagulation and leucoderma [4-5], respectively. It inhibits oncogene-induced transformation of murine fibroblasts [6]. It has been reported to posses antitumor [7], aldose reductase inhibitor [8] and xanthine oxidase inhibitor [9] activities. It also reduces blood glucose levels [10]. With all these considerations in mind, we have synthesized 7-Benzoyloxycoumarin whose structure was established by ^{1}H NMR data and finally confirmed by X-ray analysis. X-ray data of 7-Benzoyloxycoumarin was undertaken in array to decide its crystal arrangement and intrinsic conformation. To the best of our knowledge there are no reports in the literature describing the synthesis and X-ray studies of title compound. Moreover, the structure of the synthesized compound is not present in the Cambridge Structural Database.

MATERIALS AND METHODS

Chemicals and solvents were of reagent grade and used without further purification. Melting points was determined by open capillary method and are uncorrected. All the reactions were monitored using Thin Layer Chromatography (TLC) in which the glass plates coated with Silica Gel G as stationary phase were used. The TLC plates were developed in Iodine Chamber. ^{1}H-NMR spectra was run in $CDCl_3$ on a Bruker AC 300 (400 MHz) with TMS as internal standard and its values are given in ppm (δ).

Synthesis

The reaction of 7-hydroxycoumarin with PCl_3 in presence of benzoic acid afforded 7-benzoyloxycoumarin (**2**) in 70% yield (Scheme **1**) using related literature method [11]. The title compound so obtained was grown as single crystal with $CHCl_3$/ Et_2OH.

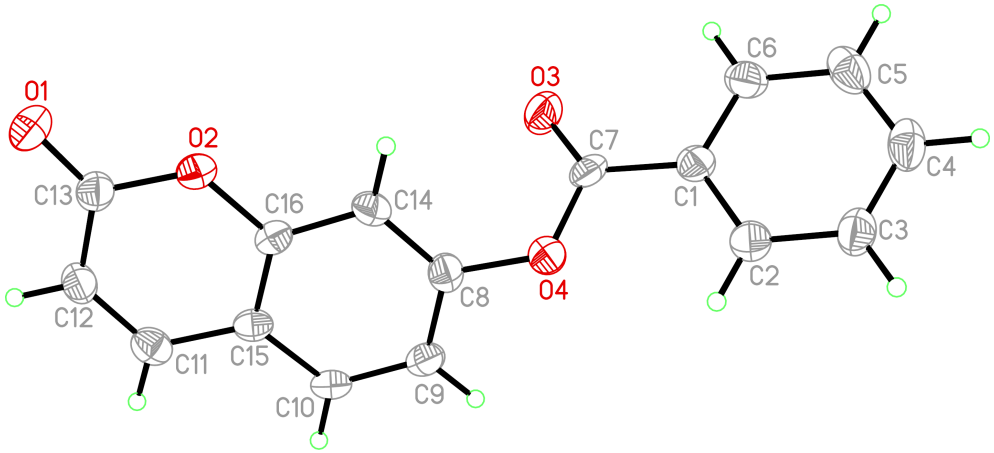

Fig.1 An ORTEP drawing of the title molecule with the atom-numbering scheme. Thermal ellipsoids are shown at 33% probability levels.

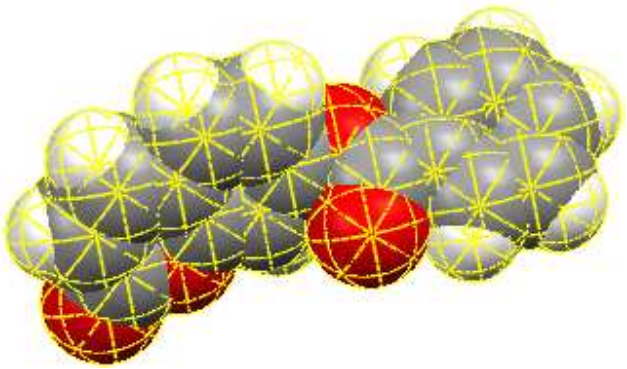

Fig.2 Space filled model of the title compound 2

Single crystal X-ray diffraction studies

A colourless needle shaped structure having dimension 0.42 x 0.12 x 0.08 mm was used for crystal data collection The three-dimensional intensity data for 7-benzoxycoumarin (mp 443 K) were collected on an Enraf-Nonius CAD-4 diffractometer using MoKα radiation (λ = 0.9917 and

0.9572 Å). The three-dimensional data were collected by using $\omega/2\theta$scan mode in the θ-range of 2.94 to 25.08^{o}. A total number of 3295 reflections were collected of which 2136 were symmetry-independent and the same number were found to be unique (-4<=h<=4, -31<=k<=33, -7<=l<=6) and 1252 as observed [I>2σ (I)].

The structure was solved by direct methods using SHELXS97 program [12]. Some non-hydrogen atoms were refined anisotropically, while the rest were refined isotropically. Hydrogen atoms were located from a difference Fourier map and refined along with all of the parameters of the non-hydrogen atoms carried out full-matrix least-squares refinement of the structure, with residual index *R* = 0.0210, by Bruker SHELXTL program. The crystal and experimental data are listed in Table 1. An ORTEP view [13] of the molecule is shown in Fig. **1** and its space fills structure in fig. **2** using MERCURY. Atomic coordinates with equivalent isotropic displacement parameters, selected bond lengths, bond angles, anisotropic displacement parameters and the hydrogen coordinates with isotropic displacement parameter are listed in Table (2-5). The hydrogen atoms were included in the final cycles of refinement; they were constrained to ride on their parent atoms. The constrained distance were C=O =1.203 ° A and C–H = 0.93 °A for all other C–H atoms.

The final cycle of refinement yielded R1 = 0.0535, wR2 = 0.0842. The maximum and minimum values for the residual electron density are 0.133 and -0.130 e.A^-3, respectively. Atomic scattering factors can be obtained from International Tables for crystallography (1992, Vol. C Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are listed in Table 1.

RESULTS AND DISCUSSION

The structure **2** crystallizes in space group *P2(1)* with 2 molecules in the unit cell packed in a head-tail fashion in rows that are roughly parallel to each other. The lactone moiety of one molecule is aligned in opposite direction of neighbouring one. Bond distances and bond angles are in agreement with some analogous structures [14]. The double bonds C13=O4 and C6=C7, are confirmed by their respective distances of 1.203(4) and 1.334(4) Å .The bonds C16-O3 [1.382(3) A°] and C13-O4 [1.382(4) Å] have variation in their distances; a feature quite common in coumarins.

The benzene ring has equivalent bonds that are within 1σ of the average value of 1.375(4) Å except for C(8)-C(14) which is 2σ below the average value. The C(13)-O(1) bond 1.203(4) Å has a normal value for a carbonyl group, the double bond character for C(11)-C(12) of 1.334(4) Å appears to be retained as for coumarin, 1.344(5) Å. The two bonds, C(12)-C(13) and C(11)-C(15) with distances 1.425(4) and 1.434(4) Å, are in reasonable agreement with the values reported in literature [15] and therefore appear to be normal for this type of ring system. The value of two C-O bonds, one in the heterocyclic ring and second bond attached to C8 of ring A are 1.382(3) and 1.391(3) Å and are in agreement with the accepted C(sp^2)-O(sp^2) distance. The external bond angles C(14)-C(16)-O(3) and C(10)-C(15)-C(11) at the junction of the two rings are smaller and greater than 120.0±, respectively, and cause O(1) to approach C(16) and C(15) to move away from C(10). The benzoyloxy group attached to 7-position of coumarin moiety are coplanar with the benzene ring. In the case of an almost coplanar benzoyloxy group, the orbitals of the O electron pairs have the greatest overlap with the p orbitals of the aromatic ring system;

due to the negative inductive effect of the benzoyloxy group as well long range electronic whirlpool, it slightly decrease bond angles and distances from respective values of coumarin. The arrays of molecules are stabilized through the numbers of different >CO….H-C, >O…H and CH….CH interactions which fall under the category of Vander Waal's interactions (fig. **3)**, and developing the three-dimensional structure. A packing diagram of the title compound is shown in figure **3**. However structural analysis of (**2**) shows that the title compound does not exist conventional hydrogen bonds and π–π stacking interactions, and therefore, the crystal packing is dominated by the Vander Waal's interactions, (fig.**4**) resulting in packing of the molecules in layers.

In the ^{1}H-NMR (400 MHz, CDcl3, measured at r.t.) spectrum of 7-benzoxycoumerin **2**, the characteristic two low field doublets at δ 6.41 and 7.1 (1H each, J=8.5 Hz) were attributed to the two olefinic protons of coumarin moiety. The aromatic protons appeared downfield singles at δ 7.53 and δ 8.20 in compound **2** and sharp single at δ5.61 attributable to the -OH group is absent in the parent coumarin.

Fig. 3. Array of molecules stabilized by different types of vander Waal's interaction.

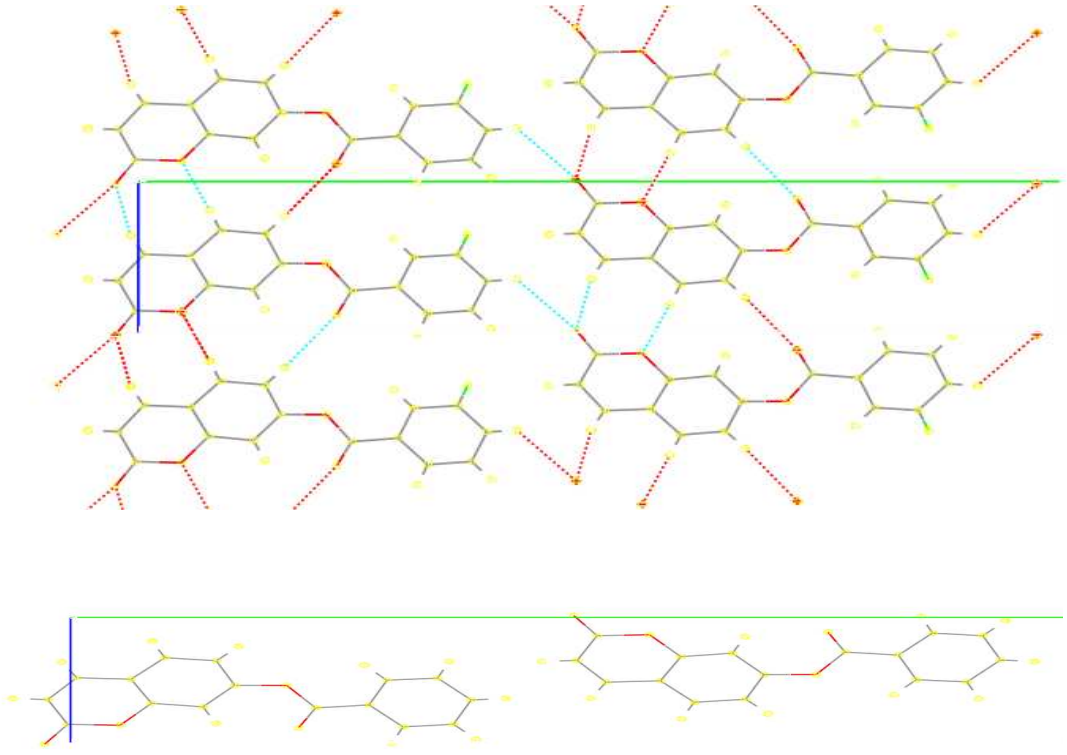

Fig.4 A partial packing diagram of 2 viewed the *a*-axis showing symmetry code (i) and (ii) correspond to [x,y,z] identity and [-x,1/2+y,-z] screw axis (2-fold), respectively.

Table 1. Crystal and Structure Refinement Data for the compound 1

Empirical formula	C16 H10 O4	
Formula weight	266.24	
Temperature	293(2) K	
Wavelength	0.71073 A	
Crystal system, space group	Monoclinic, P2(1)	
Unit cell dimensions	a = 3.8479(7) A	alpha = 90 deg.
	b = 27.693(5) A	beta = 91.056(3) deg.
	c = 5.7259(10) A	gamma = 90 deg.
Volume	610.05(19) A^3	
Z, Calculated density	2, 1.449 Mg/m^3	
Absorption coefficient	0.105 mm^-1	
F(000)	276	
Crystal size	0.42 x 0.12 x 0.08 mm	
Theta range for data collection	2.94 to 25.86 deg.	
Limiting indices	-4<=h<=4, -31<=k<=33, -7<=l<=6	
Reflections collected / unique	3295 / 2136 [R(int) = 0.0210]	
Completeness to theta = 25.86	98.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9917 and 0.9572	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2136 / 1 / 182	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.0842	
R indices (all data)	R1 = 0.0749, wR2 = 0.0916	
Absolute structure parameter	0.1(14)	
Extinction coefficient	0.000(3)	
Largest diff. peak and hole	0.133 and -0.130 e.A^-3	
CCDC No.	726153	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for 2. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	7039(8)	2819(1)	6994(6)	44(1)
C(2)	8665(8)	2988(1)	5022(6)	52(1)
C(3)	9544(9)	3466(1)	4846(6)	59(1)
C(4)	8833(10)	3783(1)	6599(7)	62(1)
C(5)	7199(10)	3617(1)	8543(7)	64(1)
C(6)	6290(8)	3140(1)	8754(5)	56(1)
C(7)	5996(8)	2315(1)	7235(5)	48(1)
C(8)	6401(8)	1550(1)	5424(6)	43(1)
C(9)	4706(8)	1377(1)	3461(5)	47(1)
C(10)	4178(8)	890(1)	3217(5)	44(1)
C(11)	4875(8)	58(1)	4822(6)	49(1)

C(12)	6113(8)	-215(1)	6567(6)	52(1)
C(13)	7945(9)	-27(1)	8552(6)	50(1)
C(14)	7582(8)	1251(1)	7146(6)	45(1)
C(15)	5342(7)	571(1)	4934(5)	40(1)
C(16)	7034(7)	764(1)	6864(5)	39(1)
O(1)	4388(6)	2154(1)	8827(4)	69(1)
O(2)	7090(6)	2043(1)	5441(4)	55(1)
O(3)	8324(5)	469(1)	8620(4)	48(1)
O(4)	9234(7)	-247(1)	10158(4)	71(1)

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for 2. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	47(2)	46(2)	39(2)	0(2)	-6(2)	5(2)
C(2)	56(2)	50(2)	48(2)	0(2)	-6(2)	-2(2)
C(3)	61(2)	55(2)	62(2)	11(2)	-6(2)	-11(2)
C(4)	69(3)	44(2)	72(3)	8(2)	-17(2)	-3(2)
C(5)	69(3)	50(2)	74(3)	-12(2)	-24(2)	12(2)
C(6)	65(2)	58(2)	44(2)	-5(2)	-7(2)	5(2)
C(7)	63(2)	47(2)	32(2)	12(2)	2(2)	7(2)
C(8)	43(2)	38(2)	48(2)	0(2)	15(2)	-3(1)
C(9)	48(2)	53(2)	38(2)	3(2)	4(2)	5(2)
C(10)	44(2)	56(2)	31(2)	-2(2)	1(2)	-2(2)
C(11)	51(2)	51(2)	47(2)	-5(2)	10(2)	-7(2)
C(12)	62(2)	39(2)	55(2)	-4(2)	11(2)	-1(2)
C(13)	55(2)	49(2)	47(2)	3(2)	15(2)	4(2)
C(14)	48(2)	48(2)	39(2)	-4(2)	-6(2)	-2(1)
C(15)	33(2)	51(2)	36(2)	0(2)	6(1)	1(1)
C(16)	38(2)	46(2)	34(2)	6(1)	2(1)	3(1)
O(1)	103(2)	52(2)	54(1)	10(1)	25(1)	7(1)
O(2)	74(2)	45(1)	47(1)	-1(1)	13(1)	-5(1)
O(3)	55(1)	52(1)	38(1)	0(1)	-6(1)	2(1)
O(4)	96(2)	61(2)	56(2)	14(1)	-2(1)	16(1)

Table 3. Bond lengths [A] and angles [deg] for 2

C(1)-C(6)	1.378(4)	C(6)-C(1)-C(2)	119.0(3)
C(1)-C(2)	1.382(4)	C(6)-C(1)-C(7)	119.1(3)
C(1)-C(7)	1.462(4)	C(2)-C(1)-C(7)	121.9(3)
C(2)-C(3)	1.373(4)	C(3)-C(2)-C(1)	120.1(3)
C(2)-H(2)	0.9300	C(3)-C(2)-H(2)	119.9
C(3)-C(4)	1.365(5)	C(1)-C(2)-H(2)	119.9
C(3)-H(3)	0.9300	C(4)-C(3)-C(2)	120.9(4)
C(4)-C(5)	1.369(5)	C(4)-C(3)-H(3)	119.5
C(4)-H(4)	0.9300	C(2)-C(3)-H(3)	119.5
C(5)-C(6)	1.371(4)	C(3)-C(4)-C(5)	118.8(3)
C(5)-H(5)	0.9300	C(3)-C(4)-H(4)	120.6
C(6)-H(6)	0.9300	C(5)-C(4)-H(4)	120.6
C(7)-O(1)	1.198(3)	C(4)-C(5)-C(6)	121.2(4)
C(7)-O(2)	1.347(4)	C(4)-C(5)-H(5)	119.4
C(8)-C(14)	1.359(4)	C(6)-C(5)-H(5)	119.4
C(8)-C(9)	1.375(4)	C(5)-C(6)-C(1)	119.9(4)
C(8)-O(2)	1.391(3)	C(5)-C(6)-H(6)	120.0
C(9)-C(10)	1.370(4)	C(1)-C(6)-H(6)	120.0
C(9)-H(9)	0.9300	O(1)-C(7)-O(2)	123.1(3)
C(10)-C(15)	1.390(4)	O(1)-C(7)-C(1)	125.1(3)
C(10)-H(10)	0.9300	O(2)-C(7)-C(1)	111.9(3)
C(11)-C(12)	1.334(4)	C(14)-C(8)-C(9)	121.9(3)
C(11)-C(15)	1.434(4)	C(14)-C(8)-O(2)	122.1(3)
C(11)-H(11)	0.9300	C(9)-C(8)-O(2)	115.8(3)
C(12)-C(13)	1.425(4)	C(10)-C(9)-C(8)	119.6(3)
C(12)-H(12)	0.9300	C(10)-C(9)-H(9)	120.2
C(13)-O(4)	1.203(4)	C(8)-C(9)-H(9)	120.2
C(13)-O(3)	1.382(4)	C(9)-C(10)-C(15)	120.5(3)
C(14)-C(16)	1.372(4)	C(9)-C(10)-H(10)	119.7
C(14)-H(14)	0.9300	C(15)-C(10)-H(10)	119.7
C(15)-C(16)	1.380(4)	C(12)-C(11)-C(15)	119.1(3)
C(16)-O(3)	1.382(3)	C(12)-C(11)-H(11)	120.5
C(16)-C(14)-H(14)	121.2	C(15)-C(11)-H(11)	120.5
C(16)-C(15)-C(10)	117.5(3)	C(11)-C(12)-C(13)	123.7(3)
C(16)-C(15)-C(11)	118.5(3)	C(11)-C(12)-H(12)	118.1
C(10)-C(15)-C(11)	124.1(3)	C(13)-C(12)-H(12)	118.1
C(14)-C(16)-C(15)	122.9(3)	O(4)-C(13)-O(3)	116.1(3)
C(14)-C(16)-O(3)	116.3(3)	O(4)-C(13)-C(12)	128.0(3)
C(15)-C(16)-O(3)	120.7(3)	O(3)-C(13)-C(12)	115.8(3)
C(7)-O(2)-C(8)	119.5(3)	C(8)-C(14)-C(16)	117.7(3)
C(16)-O(3)-C(13)	122.2(2)	C(8)-C(14)-H(14)	121.2

Symmetry transformations used to generate equivalent atoms:

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for 2

	x	y	z	U(eq)
H(2)	9164	2776	3812	62
H(3)	10641	3576	3513	71
H(4)	9448	4107	6475	74
H(5)	6695	3830	9743	77
H(6)	5168	3033	10084	67
H(9)	3924	1589	2307	56
H(10)	3031	772	1892	52
H(11)	3726	-83	3551	59
H(12)	5761	-547	6483	62
H(14)	8722	1371	8468	54

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