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Ethyl-8-ethoxy-2-oxo-2*H*-chromene-3-carboxylate: Synthesis, characterization, crystal and molecular structure and Hirshfeld surface analysis

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ABSTRACT

The title compound ethyl-8-ethoxy-2-oxo-2H-chromene-3-carboxylate has been synthesized by Knoevenagel condensation reaction. The product obtained was characterized by IR, ^{1}H NMR, MS spectral analysis and finally the crystal and molecular structure was determined by single crystal X-ray diffraction studies. The compound crystallizes in the monoclinic crystal system, in $P2_1/n$ space group with unit cell parameters a = 7.5355(6) Å, b = 17.9307(14) Å , c = 9.9423(8) Å, β = 100.974(3)º, Z = 4, V = 1318.81(18) Å^3. The structure exhibits an inter-molecular hydrogen bond of the type C-H…O. Hirshfeld analysis was carried out in order to understand the packing pattern and intermolecular interactions. Further, the Hirshfeld analysis demonstrates the predominant participation of the carbonyl-O atom as the hydrogen bond acceptor.

Keywords: Coumarins, Crystal Structure, X-ray diffraction, Extended conformation, Hirshfeld Surfaces, C-H…O interaction**.**

INTRODUCTION

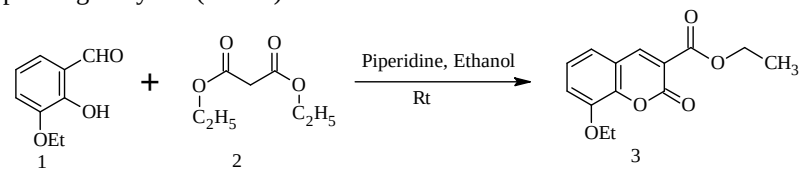
Coumarin has been identified as an important compound in the area of photochemistry,especially as a building block in the crystal lattice for photo-cycloaddition reactions [1]. They play a vital role as key constituent in a number of biologically active molecules. Synthetic coumarins are useful as anti-coagulants, coronary dialators, anti-bacterial, anti-fungal and plant growth inhibitors. Recently, coumarin compounds are described as anti-HIV and iron chelators with fluorescent sensors [2]. They have been found to possess a wide variety of uses in the perfume industry, as flavour enhancers, sunscreens, laser dyes and in the pharmaceutical industry [3]. With these considerations and as a part of our ongoing research on novel heterocyclic carboxylates [4-7], we report herein the synthesis and crystal structure of ethyl 8-ethoxy-2-oxo-2*H*-chromene-3-carboxylate which has been used as key intermediate in developing of many coumarin based dyes for material applications. Further, Hirshfeld surface analysis including d_{norm} surfaces and 2D Fingerprint plots (FP) were performed and the results of the analysis are discussed.

MATERIALS AND METHODS

Commercially available chemicals were used without further purifications.^{1}H NMR was recorded at 400MHz in Dimethylsulfoxide (DMSO-d_6). ^{13}C NMR was recorded at 100MHz in DMSO-d_6. Mass spectra was recorded on a Jeol SX 102=DA-6000 (10 kV) mass spectrometer. Melting point was determined in open capillary tube.

Synthesis

A mixture of 3-ethoxysalicylaldehyde (2 g, 11.48 mmol) and diethylmalonate(1.83 g, (11.48mmol) were dissolved in ethanol (25 ml), followed by addition of catalytic amount of piperidine. This reaction mixture was stirred at room temperature for 3 hrs . The completion of the reaction was monitored by thin layer chromatography [petroleum ether and ethyl acetate (8:2 v/v)]. After completion of the reaction, the reaction mixture was added to the ice cold water, acidified with dilute hydrochloric acid to neutralize the piperidine. The product separated out from the reaction mixture was filtered and washed with water. The crude product was further purified by recrystallization by using methanol as solvent and upon slow evaporation of methanol white crystals of ethyl 8-ethoxy-2-oxo-2*H*-chromene-3-carboxylate developed in good yield (80.5%). M.P = 96-98^{0}C.



Scheme-1: Knoevenagel synthesis of ethyl 8-ethoxy-2-oxo-2*H*-chromene-3-carboxylate

X-ray crystallographic study

The X-ray intensity data were collected at a temperature of 296.1(5) K on a Bruker Proteum2 CCD diffractometer equipped with an X-ray generator operating at 45 kV and 10 mA, using Cu-Kα radiation of wavelength 1.54178 Å. Data were collected for 24 frames per set with different settings of φ (0^o and 90^o), keeping the scan width of 0.5^o, exposure time of 5 s, the sample-to-detector distance of 45.10 mm, and 2θ value at 46.6^o. Image processing and data reduction were done using SAINT-Plus and XPREP [8]. The structure was solved by direct methods using SHELXS-97 [9]. All the non-hydrogen atoms were revealed in the first-difference Fourier map itself and were refined anisotropically. All the hydrogen atoms were positioned geometrically. In 1 and 2, the C_{arm}-H atoms were positioned geometrically, with C-H = 0.93 Å, and refined using a riding model with U_{iso}(H) = 1.2 U_{eq}(C). The crystallographic data and refinement parameters are given in Table 1. All the geometrical calculations were carried out using the program *PLATON* [10]. The molecular and packing diagrams were generated using the software *MERCURY* [11].

Table 1: Crystal data and structure refinement table

Parameter	Value
CCDC deposit No.	CCDC 1447837
Empirical formula	$C_{14}H_{14}O_5$
Formula weight	262.25
Temperature	293(2) K
Wavelength	1.54178 Å
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a = 7.5355(6) Å b = 17.9307(14) Å, c = 9.9423(8) Å β = 100.974(3)º
Volume	1318.81(18) Å^3
Z, Calculated density	4, 1.321 Mg/m^3
Absorption coefficient	0.846 mm^{-1}
$F_{(000)}$	522
Crystal size	0.29 x 0.27 x 0.24 mm
Theta range for data collection	6.47º to 64.58°
Limiting indices	-8≤ h ≤ 8, -20 ≤ k ≤ 20, -3 ≤ l ≤ 11
Reflections collected / unique	2169/ 2169 [R(int) = 0.0000]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2169 / 0 / 175
Goodness-of-fit on F^2	1.088
Final R indices [I>2σ(I)]	$R1$ = 0.0431, $wR2$ = 0.1186
R indices (all data)	$R1$ = 0.0508, $wR2$ = 0.1250
Largest diff. peak and hole	0.129 and −0.155 e. Å^{-3}

Hirshfeld surface calculations

Hirshfeld surface analyses were carried out and finger print plots were plotted using the software CrystalExplorer 3.0 [12]. The d_{norm} plots were mapped with colour scale in between −0.18 au (blue) and 1.4 au (red). The 2D fingerprint plots [13, 14] were displayed by using the expanded 0.6–2.8 Å view with the d_e and d_i distance scales displayed on the graph axes. When the cif file was uploaded into the CrystalExplorer software, all bond lengths to hydrogen were automatically modified to typical standard neutron values i.e., C–H = 1.083Å.

The ORTEP of the title compound with thermal ellipsoids drawn at 50% probability is shown in **Figure 1**.

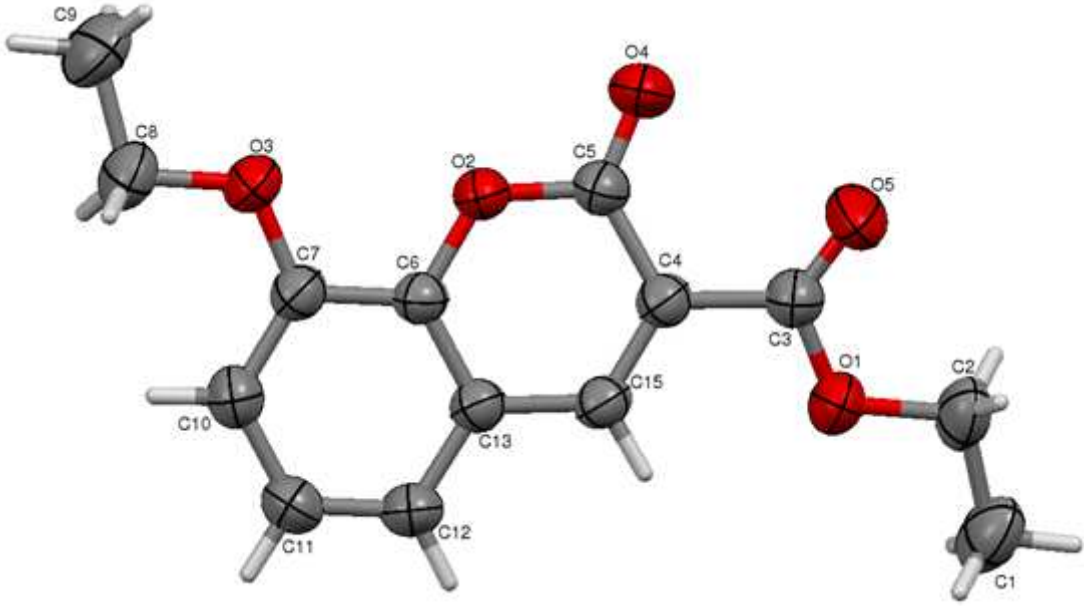


Figure 1: ORTEP of the molecule with thermal ellipsoids drawn at 50% probability

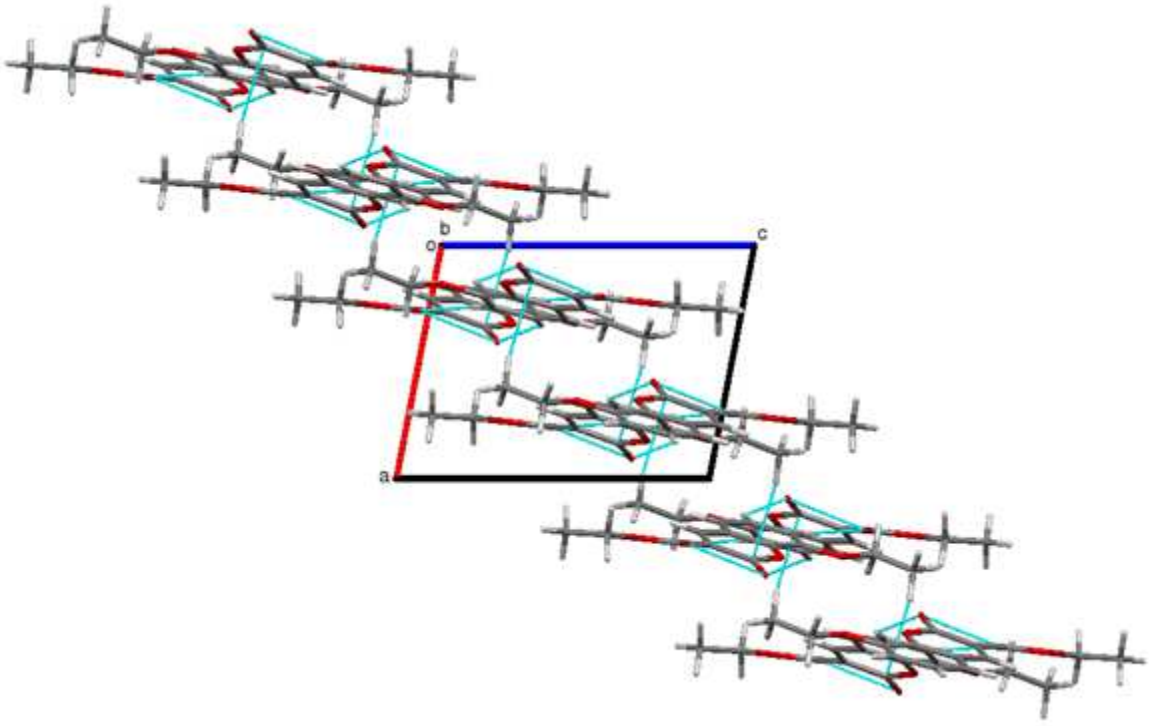


Figure 2: Packing of the molecules when viewed down along the *b* axis. The dotted line represents intermolecular hydrogen bonds

The bond lengths and bond angles are in good agreement with the standard values. The coumarin core has a planar conformation. The dihedral angle between the two six membered rings is 4.38^{o}. The pendant ethyl chain has an extended conformation as indicated by the torsional angle value of -176.89(17)^{o} for C3-O1-C2-C1. The ethyl chain is twisted out of the coumarin ring plane as indicated by the torsion angle values of 15.7(2)^{o} and -165.06(15)^{o} for C15-C4-C3-O1 and O1-C3-C4-C5 respectively. Electron localization was found at the short C4-C15 bond with a length of 1.343(2) Å. The coplanar ethoxy group lies in the plane of the coumarin ring and has a *trans* conformation as indicated by the torsion angle value of -177.59(18)^{o} for C7-O3-C8-C9. The structure exhibits an inter-molecular hydrogen bond of the type C—H...O. The C10—H4...O5 hydrogen bond has a length of 3.358(2) Å and an angle of 178^{o} with a symmetry code *1/2-x,1/2+y,1/2-z*. The packing of the molecules when viewed down along the *b* axis indicates that the molecules exhibit sheet like arrangement (**Figure 2**).

Hirshfeld surface studies

Hirshfeld surface analysis is an effective tool for exploring packing modes and intermolecular interactions in molecular crystals, as they provide a visual picture of intermolecular interactions and of molecular shapes in a crystalline environment. Surface features characteristic of different types of intermolecular interactions can be identified, and these features can be revealed by colour coding distances from the surface to the nearest atom exterior (d_e plots) or interior (d_i plots) to the surface. This gives a visual picture of different types of interactions present, and also reflect their relative contributions from molecule to molecule. Further, 2D fingerprint plots (FP), in particular the breakdown of FP into specific atom…atom contacts in a crystal, provide a quantitative idea of the types of intermolecular contacts experienced by molecules in the bulk and presents this information in a convenient colour plot. Hirshfeld surfaces comprising d_{norm} surface and Finger Print plots were generated and analysed for the title compound in order to explore the packing modes and intermolecular interactions. The two dimensional fingerprint plots from Hirshfeld surface analyses **Figure 3**, illustrates the difference between the intermolecular interaction patterns and the relative contributions to the Hirshfeld surface (in percentage) for the major intermolecular contacts associated with the title compound. Importantly, H...H (38.8%) bonding appears to be a major contributor in the crystal packing, whereas the O...H, C...H, C...O plots also reveal the information regarding the intermolecular hydrogen bonds thus supporting for C--H...O intermolecular interactions. This intermolecular contact is highlighted by conventional mapping of d_{norm} on molecular Hirshfeld surfaces and is shown in **Figure 4**. The red spots over the surface indicate the intercontacts involved in hydrogen bond. The dark-red spots on the d_{norm} surface arise as a result of the short interatomic contacts, i.e., strong hydrogen bonds, while the other intermolecular interactions appear as light-red spots.

SUPPLEMENTARY MATERIALS: CCDC 1447837 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk.

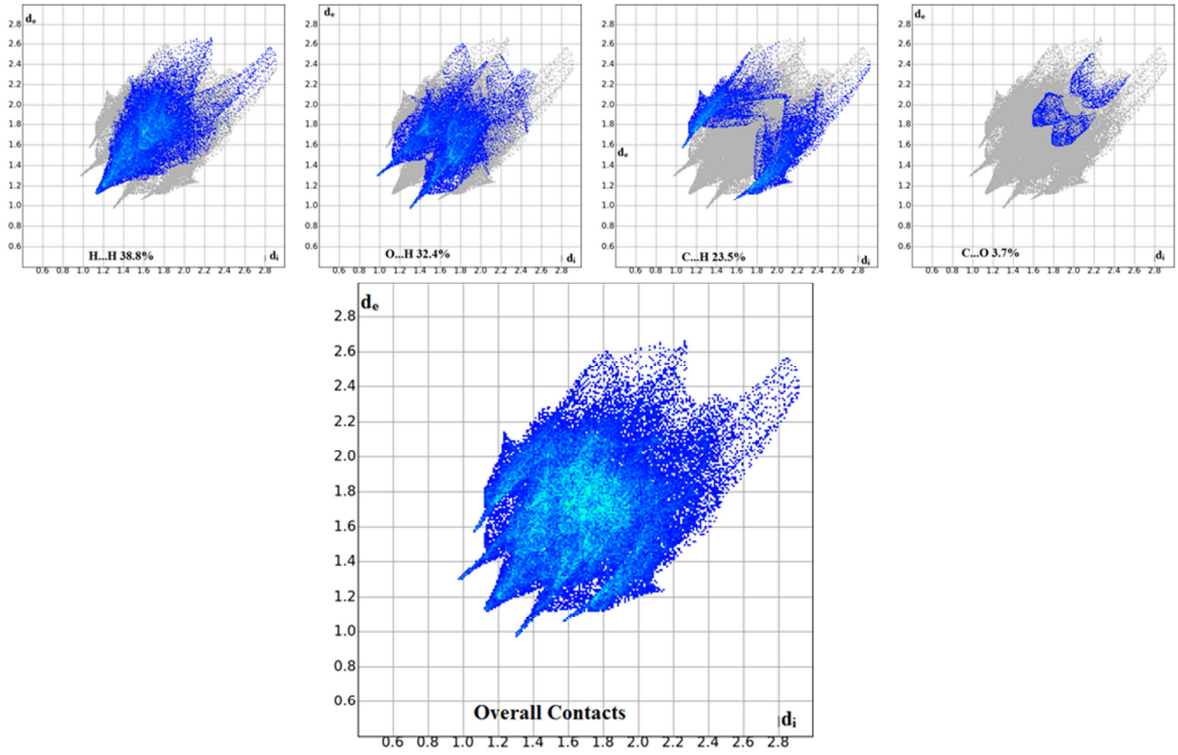


Figure 3: Fingerprint plots of the title compound showing H...H, O…H, C...H and C...O interactions. d_i is the closest internal distance from a given point on the Hirshfeld surface and d_e is the closest external contacts

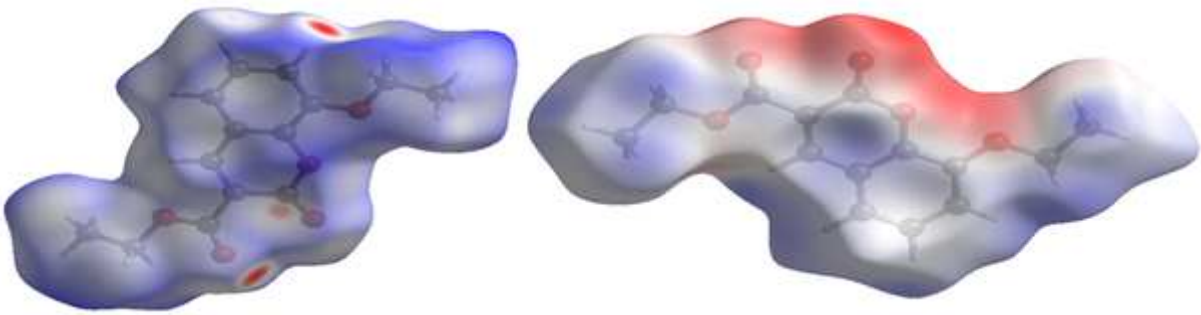


Figure 4: d_{norm} and electrostatic potential mapped on Hirshfeld surface for visualizing the intermolecular contacts

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