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# Synthesis, crystal structure, Hirshfeld surface analysis and DFT calculations of 2, 2, 2-tribromo-1-(3,5-dibromo-2-hydroxyphenyl)ethanone



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# ABSTRACT

A novel derivative 2, 2, 2-tribromo-1- (3,5-dibromo-2-hydroxyphenyl) ethanone was synthesis by "3acetyl-4-hydroxycoumarin" and dibromide. The structural properties of the synthesized compound have been exploited with the aid of single-crystal X-ray crystallographic studies and infrared spectrometry. The compound crystallizes in the monoclinic system with space group P2<sub>1</sub>/c. A comparative study between the novel brominated compound synthesized and the brominated coumarin derivative is presented. The optimized DFT geometries (B3PW91/6-311 G (2df, p)) and the spectral simulations of two derivatives compared agree well with the experimental data. Hirshfeld's analysis revealed the importance of Br ... Br (40%) and Br ... H/H ... Br (19%) of the total surface contacts in the molecular stack. The contacts 0...H/H...O have a significant contribution for the brominated coumarin (*C2*) of 26.1% of SH compared to the brominated cycle (*C1*) 9.7%.

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# 1. Introduction

Brominated coumarins present a wide range of biological activities and important applications in pharmaceuticals, due to their occurrence in nature [1]. Coumarin derivatives are sensitive to electrophilic substitution [2]; their reaction with Bromine can give rise to several compounds used as intermediate products sensitive to interesting substitutions in a wide range of organic syntheses [3]. The bromination of these compounds increases their anticonvulsant activity [4], which convert them pharmacological importance. They also have interesting biological properties as powerful antioxidants, as well as acceptable antimicrobial and antituberculosis activities [5]. Coumarins containing halogens have insecticidal and fungicidal properties [6].

Brominated coumarins were used as synthetic precursors of furocoumarins and furocoumarins dihydro, which are widely used

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as photosensitizers and chemotherapeutic agents to fight skin diseases [7]. Rao and Kumar also claimed that the bromination of coumarin increases its reactivity and promotes chemoselective reactions [8]. Bromo-coumarins are used as starting reagent in the preparation of 3-arylcoumarins [2–10], 1,3,4-oxadiazole derivatives, and benzofuran-2-carboxylic acids by a Perkin rearrangement reaction [11]. Therefore, the synthesis of brominated 3aminocoumarins becomes very interesting among organicists. Recent research suggests that Bromo-coumarins also have powerful optical and biological properties and they could increase the reactivity of coumarins and favor chemo selective reactions. In this context, our research group recently reported the synthesis of a new brominated derivative prepared from 3-acetyl-4hydroxycoumarin. The molecular structure was carried out by Xray crystallography, Hirschfeld surfaces analysis, and DFTB3LYP method with the basis set 6-311++G (d,p). Additionally, the UV-Vis spectroscopic behavior of this derivative in different solvents was investigated. The present study concerns the structural comparison and the biological activity of new brominated compound and brominated coumarin already studied [12].

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# 2. Experimental

### 2.1. Infrared and UV-visible spectroscopies

The starting compound '3-acetyl-4-hydroxycoumarin' was prepared as previously described [13]. The IR spectrum was recorded on a Bruker FT-IR spectrophotometer Tensor 27 by KBr pellet technique in the range 4000–400 cm<sup>-1</sup>. The electronic absorption spectra were recorded on double beam UVD-3500 UV-Vis spectrometer in methanol and ethyl acetate in the region 200–900 nm.

### 2.2. Hirshfeld surface analysis

The Hirshfeld surface becomes a valuable tool for analyzing the intermolecular interactions of an entire molecule. It is defined by the isosurface 0.5 of the weight function w(r) (Eq. 1). The sum of the electron densities of spherical atoms of the molecule (the promolecule) divided by the same sum for the crystal (the procrystal) inside the surface of Hirshfeld, the electron density of the promolecule dominates the procrystal [13].

By defining a function of molecular weight w(r):

$$\omega(\mathbf{r}) = \frac{\rho \text{ promoécule}(\mathbf{r})}{\rho \text{ procristal}(\mathbf{r})} = \frac{\sum \rho A(r)[A \in molécule]}{\sum \rho A(r)[A \in cristal]}$$

 $\rho A$  (r): the average electron density of an atomic nucleus A centered on this nucleus.

For a point on the surface, the distances to the nearest atoms outside,  $d_e$ , and inside,  $d_i$ , are easily defined and are used as properties, can define the identity of these atoms and to explore intermolecular contacts in a crystal.

In addition, a normalized contact distance,  $d_{norm}$  (Eq. 2), is defined where  $r^{vdW}$  is the van der Waals radius (vdW) of the appropriate internal or external atom at the surface.

$$d_{norm} = rac{d_i - r_i^{
u dW}}{r_i^{
u dW}} + rac{d_e - r_e^{
u dW}}{r_e^{
u dW}}$$

The intermolecular interactions of the present simple are quantified using Hirshfeld surface analysis. The program CrystalExplorer 3.1 [14] established the Hirshfeld surface analyzes by introducing into this software a file of the studied structure in CIF format.

# 2.3. Quantum chemical calculations

The B3LYP [15,16] and M06-2X [17] calculations were performed by G09W [18] package, in the gas, DMSO and Water phases, at 6-311++G(d,p) basis set. The gas-phase optimized and verified structure of the compound, which had no imaginary frequency, was been used for the solvent media calculations. For the solvent environment calculations, the PCM (polarized continuum model) was used [19,20]. The vibrational mode assignment of the compound has been performed by PED (potential energy distribution) analysis by VEDA [21], and the O-H and aromatic C-H frequencies have been scaled down [22] by the factor 0.960 for B3LYP/6-311++G(d,p) level. The NBO (natural bond orbital) [23,24] investigation has conducted to evaluate the structureintramolecular interactions relationship. The FMO (frontier molecular orbital) analysis [25–28] has been used to evaluate the chemical reactive behavior of the compound by using the DFT-based reactivity descriptors.

Conceptual Density Functional Theory [29] based equations are widely used in the calculation of quantum chemical descriptors like hardness, softness, electronegativity and chemical potential. The relation with total electronic energy, number of electrons, ionization energy and electron affinity of the mentioned reactivity descriptors are presented via the following equations [30].

$$\mu = -\chi = \left[\frac{\partial E}{\partial N}\right]_{\nu(r)} = -\left(\frac{I+A}{2}\right)$$
$$\eta = \frac{1}{2} \left[\frac{\partial^2 E}{\partial N^2}\right]_{\nu(r)} = \frac{I-A}{2}$$
$$\sigma = 1/\eta$$

As can be seen from the equations given above, to calculate the quantum chemical descriptors given, we need to ionization energy and electron affinity parameters. It is important to note the ionization energy and electron affinity values of molecules can be predicted with the help of frontier orbital energies in the light of Koopmans Theorem [31]. The theorem states that negative values of HOMO and LUMO orbital energies of any molecule correspond to ionization energy and electron affinity values of the aforementioned molecule

$$I = -E_{HOMO}$$

 $A = -E_{LUMO}$ 

Parr, Szentpaly and Liu [32] modeled the electrophilicity index based on electronegativity (or chemical potential) and chemical hardness of any chemical species via the following equation.

$$\omega = \chi^2 / 2\eta$$

Then, Chattaraj [33] proposed that nucleophilicity can be given as the multiplicative inverse of electrophilicity index as  $\varepsilon = 1/\omega$ . Polarizability [34] that is one of the useful reactivity descriptors is calculated depending on diagonal components of polarizability tensor.

$$\langle \alpha \rangle = 1/3[\alpha_{xx} + \alpha_{yy} + \alpha_{zz}]$$

2.4. General procedure for synthesis of the brominated derivatives (C1) and (C2)

An excess of dibroma (10 equivalent) dissolved in acetic acid was added dropwise to a solution of 3-acetyl-4-hydroxy-2H-chromene-2-one in acetic acid. During the reaction, the dropwise addition was carried out after each disappearance of the brown coloration of the dibroma (Br<sub>2</sub>). The reaction mixture was kept stirring at 373 K until the brown color persisted. The solution obtained was crystallized at room temperature to obtain a crystalline powder containing two types of crystals, the first of the transparent colorless crystals with a melting temperature equal to 393 K and



Fig. 1. The infrared absorption spectra of C1 and C2.



Fig. 2. The UV-Visible spectra of C1:(a) and C2:(b) in different solvents.

68% yield (assigned to **C1** in the present work), and, the second yellow, with a melting temperature equal to 388K and 32% yield (assigned to **C2** [12] in the present work).

# 3. Results and discussion

# 3.1. Infrared spectroscopy

The infrared spectrum of the pentabromo-derivative (*C1*) "2,2,2-tribromo-1- (3,5-dibromo-2-hydroxyphenyl) ethanone" (Fig. 1) shows a band around 3170 cm<sup>-1</sup> which can be attributed to the valence vibration of the OH bond ( $\nu$ OH) of the hydroxyl group. Also,  $\nu$ OH stretching mode has been assigned as a pure mode (99%) at 3263 cm<sup>-1</sup> with very strong intensity (Table S1: Supplementary material). The bands corresponding to the valence vibrations of the aromatic C-H bonds that appeared around 3099 and 3043 cm<sup>-1</sup> have been predicted in 3130 (99% PED) and 3087cm<sup>-1</sup> (100% PED). and that of C-C stretching vibration revealed around 1015 cm<sup>-1</sup>. The bands of elongation observed around 1713, 1651 and 1264 cm<sup>-1</sup> can be attributed, respectively to the vibrations of the C=O ketone ( $\nu$ C=O), C=C aromatic ( $\nu$ CC) and C-O bonds ( $\nu$ C-

O) of the hydroxyl group. On the other hand, the ketonic group  $\nu$ C=O and the hydroxyl group ( $\nu$ C-O) modes for **C1** molecule have been assigned as a pure mode in 1689 and 1300  $\text{cm}^{-1}$ . Besides, the ketonic group  $\nu$ C=O mode has contributed (11%) to the aromatic  $\nu$ CC (36%) and ipb HCC (in-plane-bending, 33%) modes in 1454 cm<sup>-1</sup>. Also, the assigned modes in 1393 and 1320 cm<sup>-1</sup> for **C1** molecule have also included the ketonic group  $\nu$ C=0 mode contribution to the ipb HCC and ipb HOC bending modes. From Table S1, the  $\nu$ C=O vibrational modes with very strong IR intensity for the C2 molecule (Fig. 1), includes two ketonic group, have been assigned as a pure mode in 1786 (85%) and 1663  $\text{cm}^{-1}$  (64%). The bands observed at 1413 and 663 cm<sup>-1</sup> can be attributed to the valence vibration of the aromatic C-C bond and the elongation vibration of the Br-C ( $\nu$ BrC) bond. In this context, the assigned mode for **C1** in 693 cm<sup>-1</sup> has contained the  $\nu$ Br-C mode contribution (60%) as mixed with the bending modes of  $\delta$ (CCC Ring+ CCO+ CCBr (10%). In addition, the assigned  $\nu$ Br-C mode in 571 cm<sup>-1</sup> has included the torsion ( $\chi$  CCCC, 10%) and the bending ( $\delta$ BrCBr, 16%) contributions. On the other hand, vBrC mode for C2 has been assigned in 552 cm<sup>-1</sup> purely and in 761 and 206 cm<sup>-1</sup> as contaminated with the bending modes. All vibrational mode assignment

Table 1	
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The experimental and theoretical UV-vis absorption characteristics of compound (C<sub>8</sub>H<sub>3</sub>O<sub>2</sub>Br<sub>5</sub>).

	Exp.(λnm)	Transitions	MO%	$\Delta E (eV)$	λ (nm)	f
C1						
Ethyl acetate	334	$H \rightarrow L$	(99%)	3.1012	399.80	0.0771
$(\varepsilon = 6.02)$	313	$H-2 \rightarrow L$	(15%)	3.9669	312.55	0.1079
		$H-1 \rightarrow L$	(81%)			
	_	$H-2 \rightarrow L$	(84%)	4.1113	301.57	0.0231
		$H-1 \rightarrow L$	(14%)			
Methanol	348	$H \rightarrow L$	(96%)	3.1996	387.50	0.0901
( <i>ε</i> =32.63)	310	$H-2 \rightarrow L$	(42%)	4.0302	307.64	0.0826
		$H-1 \rightarrow L$	(53%)			
	_	$H-2 \rightarrow L$	(57%)	4.1439	299.20	0.0698
		$H-1 \rightarrow L$	(38%)			
C2						
Ethyl acetate	335	$H \rightarrow L$	(97%)	3.5484	349.41	0.1163
(ε=6.02)	331	$H-1 \rightarrow L$	(54%)	3.9123	316.91	0.2245
		$H-3 \rightarrow L$	(11%)			
		$H-4 \rightarrow L$	(24%)			
	311	$H-1 \rightarrow L$	(42%)	3.9834	311.25	0.1938
		$H-3 \rightarrow L$	(22%)			
		$H-4 \rightarrow L$	(24%)			
Methanol	335	$H \rightarrow L$	(94%)	3.6212	342.38	0.1182
( <i>ε</i> =32.63)	331	$H-1 \rightarrow L$	(11%)	3.9492	313.95	0.0588
. ,		$H-3 \rightarrow L$	(25%)			
		$H-4 \rightarrow L$	(44%)			
	311	$H-1 \rightarrow L$	(75%)	4.0794	303.93	0.4577
		$H-3 \rightarrow L$	(11%)			



Fig. 3. HOMO and LUMO amplitudes contributed to the electronic transitions (isoval:0.02) of C1 and C2 molecules at B3LYP/6-1+G(d,p) level in the methanol.

details of the compound can be found in Table S1. These attributions show all the bonds of the expected molecular structure, the subsequent analysis by X-ray diffraction can specify the exact structure.

### 3.2. Ultraviolet-visible characterization

The ultraviolet-visible spectroscopy of **C1** and **C2** derivatives was studied through dilute solutions of methanol and ethyl acetate, with the concentration  $1.3 \times 10^{-5}$  M. The choice of solvents was based on the difference in polarity and the ability to form hydrogen bonds. The recorded spectra and characterization of the electronic transitions of both **C1** and **C2** were given in Fig. 2 and Table 1, respectively.

Besides, TD-DFT/B3LYP/6-311G(d,p) [35–37] calculations were conducted to characterize the electronic transition in the UV-Vis spectrum of the compound ( $C_8H_3O_2Br_5$ ). Table 1 disclosed the electronic transitions, molecular orbital contributions to the relevant transition, the energy gap between the singlet states, and oscillator strength. As reported in the past, the theoretical peaks of interest chemical species have been calculated greater 30-40 nm approximately than the observed data [38-40].

Accordingly, the UV-Vis spectrum of compound C1 revealed two peaks in 348 and 310 nm in methanol and in 334 and 313 nm in ethyl acetate. Furthermore, the first peak of C1 calculated in 399.80 nm in ethyl acetate and 387.50 nm in methanol sourced from the  $\pi \rightarrow \pi^*$  transition was related to mostly  $H \rightarrow L$  transition (99%). From Table 1, the second peak of compound C1 was calculated at 312.55 nm and overlap with the electronic transition calculated at 301.57 nm, which both transitions were due to the H-2  $\rightarrow$ L and H-1  $\rightarrow$ L and characterized by the n $\rightarrow$  $\pi^*$  interaction. Besides, the first excitation for C2 came from  $H \rightarrow L$  were calculated at 349.41 in ethyl acetate nm and 342.38 nm in methanol and appeared in 335 nm of the spectrum. From Table 1, the second peak of C2 observed in 331 nm was predicted in ethyl acetate in 316.91 nm (f= 0.2245) that was due to the mainly H-1  $\rightarrow$ L (54%), as well as the transitions of H-3  $\rightarrow$ L (11%) and H-4  $\rightarrow$ L (24%). Also, the third summit on the spectrum of C2 was 311 nm in both the ethyl acetate and methanol and calculated as 311.25 nm (f=0.1938) in ethyl acetate and in 303.93 nm in methanol, caused by

### Table 2

The second order	perturbation theory	y analysis of fock	matrix in NBO	basis of C1 and	d C2 molecules a	t B3LYP/6311++G(d,p	) level in the g	gas phase
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Donor(i)	ED <sub>i</sub> /e	Acceptor (j)	ED <sub>j</sub> /e	E <sup>(2)</sup> /kcal/ mol	E(j)-E(i)/ a.u	F(i.j)/ a.u
C1						
$\pi$ C1-C2 (2)	1.71764	π* C5-C6	0.33446	22.80	0.29	0.073
$\pi$ C5-C6 (2)	1.71509	π* C1-C2	0.33733	14.30	0.30	0.059
$\sigma$ C12-Br15 (1)	1.97755	π* C11-O13	0.21723	2.52	0.63	0.038
$\sigma$ C12-Br16 (1)	1.97756	π* C11-O13	0.21723	2.52	0.63	0.038
LP (3) Br17	1.94180	π* C1-C2	0.33733	9.66	0.30	0.052
LP (3) Br18	1.93000	π* C5-C6	0.33446	10.25	0.29	0.052
C2						
$\pi$ C1-C2 (2)	1.67625	π* C3-C4	0.43328	24.28	0.27	0.075
		$\pi^*$ C5-C6	0.26965	15.91	0.29	0.062
$\pi$ C3-C4 (2)	1.61117	π* C1-C2	0.29216	14.46	0.30	0.060
		$\pi^*$ C5-C6	0.26965	18.96	0.31	0.070
		π* C9-C12	0.36230	10.64	0.63	0.073
$\pi$ C5-C6 (2)	1.68763	π* C1-C2	0.29216	21.68	0.28	0.070
		π* C3-C4	0.43328	17.11	0.27	0.063
$\pi$ C9-C12 (2)	1.67127	π* C3-C4	0.43328	8.38	0.29	0.045
		π* C13-O17	0.29596	12.23	0.72	0.084
		π* C18-O21	0.25480	20.28	0.45	0.087
$\sigma$ C19-Br22 (1)	1.98501	π* C13-O17	0.29596	3.51	1.05	0.058
		π* C18-O21	0.25480	3.11	0.79	0.047
$\sigma$ C19-Br23 (1)	1.96759	π* C18-O21	0.25480	1.56	0.76	0.032
LP (2) O16	1.74807	π* C3-C4	0.43328	31.34	0.35	0.098
		π* C13-O17	0.29596	15.24	0.78	0.098
LP (3) Br23	1.94473	π* C18-O21	0.25480	1.31	0.45	0.023

\*  $E^{(2)} = \Delta E_{ij} = qi \frac{(Eij)^2}{(\varepsilon_j - \varepsilon_l)}$  shows the lowering of stabilization energy, where qi is the donor orbital occupancy,  $\varepsilon_i$ , and  $\varepsilon_j$  are donor and acceptor orbital energies (diagonal elements), and Fij is the off-diagonal NBO Fock matrix element.

the  $n \rightarrow \pi^*$  excitations. The results of the electronic spectra of both compounds disclosed that there were a significant hypsochromic effect for **C1** and hyperchromic effect for **C2**.

In addition, the FMOs density for  $s_1 \leftarrow s_0$  electronic transitions that occurred in both compounds were given in Fig. 3. For compound **C1**, the first excitation has taken place from the Br and – OH substituted phenyl ring, towards the aliphatic bonded two Br atoms and the whole aromatic ring, and this excitation was mainly associated with the  $\pi \rightarrow \pi^*$  transition. Besides, the second peak was due to the electronic excitations H-1 $\rightarrow$  L and H-2 $\rightarrow$  L, namely, the electron density on the excited state for H-1 was distributed on the  $-\pi$  and non-bonding orbitals whereas it for H-2 was mainly on the non-bonding orbital and partially aromatic ring. Here, H-1 and H-2 states could be associated with the  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$ interactions, respectively. For compound **C2**, the first electronic excitation was calculated for the H $\rightarrow$  L transition with the energy

# **Table 3** The crystallographic data, the conditions of intensity collection and the refinement of $C_8H3O_2Br_5$ (C1).

Chemical formula	$C_8H_3O_2Br_5$
Molecular weight	530.6
Crystal system	Monoclinic
Space group	P2 <sub>1</sub> /c
Temperature (K)	293
a, b, c (Å)	10.1770 (6), 10.2843 (6), 12.1938 (9)
β(°)	107.143(6)°
V (Å <sup>3</sup> )	1219.5(2)
Ζ	4
Radiation type	Cu <i>Kα</i>
Density (mm <sup>-1</sup> )	2,885
Diffractometer	Oxford diffraction Gemini diffractometer with
	four circles, an Atlas CCD detector
Scan range [°]	$\theta_{\max} = 66.9^{\circ}$ , $\theta_{\min} = 5.4^{\circ}$
F(000)	968
$R[F^2 > 2s(F^2)], wR(F^2), S$	0.029, 0.040, 1.11
No. of reflections	2071
No. of parameters	136
H-atom treatment	H-atom parameters constrained

gap 3.6212 eV, and it is clear that this transition could be also the  $\pi \rightarrow \pi^*$  transition because both H and LUMO were largely distributed over the  $\pi$ -conjugate system. Moreover, the second peak for C2 observed at 331 nm was associated mainly with the states H-4 $\rightarrow$  L (44%), H-3 $\rightarrow$  L (25%), and H-1 $\rightarrow$  L (11%). From Fig. 3, the H-3 and H-4 amplitudes were greatly spread out on the -Br atoms, which could be a sign of the n $\rightarrow \pi^*$  interaction, whereas H-1 $\rightarrow$ L transition characterized as  $\pi \rightarrow \pi^*$  transition also contributed to the second peak.

Furthermore, the important electron delocalization between the donor and acceptor molecular orbitals, which each contributes to the stabilization energy lowering, has been predicted by using the NBO analysis. NBO analysis has been successfully applied to explain the properties of the relevant chemical species such as stability, polarization, and electronic transitions, etc [41–43]. Thus, the results obtained from the NBO analysis summarized in Table 2 the important interactions that occurred in the compounds of relevance. Based on the results of the C1 molecule, the highest contribution to the lowering of the stabilization energy has been calculated for the electron delocalization from the  $\pi$  C1-C2 bonding orbital to  $\pi^*$  C5-C6 anti-bonding orbital, with the energy of 22.80 kcal/mol. Also, the perturbative energy for  $\pi$  C5-C6 $\rightarrow$   $\pi^*$  C1-C2 resonance interaction of the C1 molecule has been calculated as 14.30 kcal/mol ( $ED_i/e=1.71509$  e). On the other hand, for the **C2** molecule, LP (2) 016 $\rightarrow \pi^*$  C3-C4 as the resonance interaction has the highest contribution to the stabilization of the molecule with  $E^{(2)}$ =31.34 kcal/mol with the remarkable orbital occupancy  $(ED_i/e=1.74807 e)$ . From Table 2, the hyperconjugative interactions  $(\sigma \rightarrow \pi^*)$  have also contributed to the stabilization energy; the sta-

Table 4
Hydrogen-bonds geometry of structure $C_8H_3O_2Br_5$ (Å, °).

D—H····A	D—H	HA	D····A	D—H…A
01-H2o102	0.82	1.97	2.578 (5)	130.46
01-H2o102i	0.82	2.32	3.024 (6)	144.91

**Symmetry code:** (i) -*x*+1, -*y*+1, -*z*+1.



Fig. 4. The molecular structure of C<sub>8</sub>H<sub>3</sub>O<sub>2</sub>Br<sub>5</sub> (C1), the displacement ellipsoids are established with a probability of 50%.

bilization energy for the electron delocalization from each of both the  $\sigma$  C12-Br15 and  $\sigma$  C12-Br16 bonding orbitals to  $\pi^*$  C11-O13 antibonding orbital for the **C1** molecule have been calculated in 2.52 kcal/mol. Also, the energies of LP (3) Br17 $\rightarrow$   $\pi^*$  C1-C2 and LP (3) Br18 $\rightarrow$   $\pi^*$  C5-C6 resonance interactions (**C1**) have been predicted in 9.66 and 10.25 kcal/mol, remarkable in terms of contributing to the stabilization energy. However, for the **C2** molecule, the stabilization energy for LP (3) Br23 $\rightarrow \pi^*$  C18-O21 interaction is found to be in 1.31 kcal/mol, which is smaller than that of the counterpart interaction calculated for the **C1** molecule.

Table 5

The selected optimized parameters of C1 and C2 molecules at B3LYP/6-311++G(d,p) level in the	ie gas phase.
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Bond Length	(Å)	Bond angle	(°)	Dihedral angle	(°)
C1					
C1-Br17	1.91	C1-C2-C3	120.7	C1-C2-C3-C4	0.0
C5-Br18	1.90	C3-C4-C5	118.6	C1-C2-C3-C11	-180.0
C12-Br14	1.96	C3-C4-09	123.7	C2-C3-C4-09	180.0
C12-Br15	1.98	C4-O9-H10	107.9	O9-C4-C5-Br18	0.0
C4-09	1.33	C4-C5-Br18	119.1	C2-C3-C11-O13	-180.0
C11-O13	1.22	C6-C1-Br17	119.0	C2-C3-C11-C12	0.0
O9-H10	0.98	C4-C3-C11	117.3	C4-C3-C11-O13	0.0
C2-H7	1.08	C3-C11-O13	121.2	C3-C11-C12-Br14	180.0
C1-C2	1.38	C12-C11-O13	116.1	C3-C11-C12-Br15	-61.3
C3-C4	1.43	C11-C12-Br14	110.3	C3-C11-C12-Br16	61.2
C3-C11	1.48	C11-C12-Br15	109.4	013-C11-C12-Br14	-0.0
C11-C12	1.57	Br14-C12-Br15	108.1	013-C11-C12-Br15	118.7
<b>C2</b>					
(2 (10 P-22	1.05	62 63 64	101.0	C1 C2 C2 C4	0.0
C19-Br22	1.95	(2-(3-(4	121.0	CI-C2-C3-C4	-0.0
CI9-Br23	1.98	C3-016-C13	123.5	(2-(3-(4-(9	-1/9./
C9-014	1.31	016-C13-C12	116.9	C3-C4-C9-014	-179.7
C18-021	1.24	012-C13-017	127.3	C13-C12-C9-014	178.8
014-H15	1.00	016-C13-017	115.8	014-C9-C12-C18	-0.6
C2-H8	1.08	C4-C9-014	116.7	C9-C12-C18-O21	2.8
C1-C2	1.39	C9-C12-C18	117.6	C3-016-C13-017	179.3
C3-016	1.36	C12-C18-C19	120.7	016-C13-C12-C18	-179.2
C13-O16	1.39	C12-C18-O21	120.5	017-C13-C12-C18	1.2
C13-O17	1.21	C19-C18-O21	118.8	C13-C12-C18-O21	-176.6
C12-C18	1.47	C18-C19-Br22	111.7	O21-C18-C19-Br22	37.5
C18-C19	1.53	Br22-C19-Br23	112.7	O21-C18-C19-Br23	-86.0

### Table 6

The quantum chemical reactivity identifiers, total electronic and free energies of C1 and C2 molecules (CH+ shows the protonated forms in the gas phase) at B3LYP/6-311++G(d,p) level.

C1	Gas	DMSO	WATER	CH+ (Gas)
HOMO (-I)	-0.25470	-0.25190	-0.25187	-0.38662
LUMO (-A)	-0.12180	-0.11694	-0.11688	-0.29890
ΔE (L-H)	3.61640	3.67245	3.67327	2.38698
μ=-(I+A)/2	-5.12255	-5.01833	-5.01710	-9.32698
η=(I-A)/2	1.80820	1.83623	1.83663	1.19349
$\omega = \mu^* \mu / 2\eta$	7.25598	6.85744	6.85257	36.44454
$\Delta Nmax = -\mu/\eta$	2.83296	2.73296	2.73168	7.81487
α (au)	209.2316520	290.838119	292.413946	214.605065
D (debye)	1.4024280	2.181652	2.196982	3.463392
ΔE (au)	-13327.8349850	-13327.841827	-13327.841940	-13328.138048
ΔG (au)	-13327.8837050	-13327.890549	-13327.890647	-13328.186995
C2				
HOMO (-I)	-0.27421	-0.26838	-0.26829	-0.40442
LUMO (-A)	-0.11872	-0.11564	-0.11560	-0.28759
ΔE (L-H)	4.23110	4.15627	4.15491	3.17911
μ=-(I+A)/2	-5.34609	-5.22486	-5.22309	-9.41528
η=(I-A)/2	2.11555	2.07813	2.07745	1.58955
$\omega = \mu^* \mu / 2\eta$	6.75490	6.56819	6.56589	27.88440
$\Delta Nmax = -\mu/\eta$	2.52704	2.51421	2.51418	5.92322
α (au)	193.4973800	266.789155	268.141813	200.686587
D (debye)	5.9767500	8.335716	8.371225	7.681388
ΔE (au)	-5872.0358690	-5872.047883	-5872.048080	-5872.353580
∆G (au)	-5872.0814130	-5872.093123	-5872.093303	-5872.398755

# 3.3. Single crystal XRD study

The crystal of this derivative was characterized by an Oxford Diffraction Gemini diffractometer with four circles using Cu K $\alpha$  radiation with a collimating mirror from a sealed X-ray tube and an Atlas CCD detector. The structure was solved by direct methods using Superflip software [44], and the refinement was carried out with JANA 2006 software [45]. The hydrogen atoms bound to carbons were geometrically fixed (C-H = 0.93 or 0.98 Å) and refined, with Uiso (H) fixed at 1.2 Ueq from the central atom. The structure was registered in the **CCDC** database under deposition number **2068709**.

The experimental details including structure refinement and data collection details for  $C_8H3O_2Br_5$  (**C1**) were summarized in Table 3. The crystal structures presented in Figs. 4–6 was Elaborated using Mercury Program (Mercury 3.5.1 (Build RC5).

The structure of this crystal (Fig. 4) is almost planar since all of the atoms, except **C1**, are essentially coplanar with a C7-C6-C8-C7 twist angle equal to  $168.4 (5)^{\circ}$  (Table 4).

The crystal stack is arranged in the form of parallel alternating layers along the axis a. The  $C_8H_3O_2Br_5$  molecules are assembled by overlapping in a head-to-tail fashion following the  $\pi$ - $\pi$  interactions between the benzene rings in a stack along the direction of the A axis presented in (Fig. 5) with a centroid-centroid distance equal to 3.722 (2) Å.

The significant intramolecular interactions between the atoms O1 … O2 (Fig.6) (donor-acceptor distance of 2.578(5) Å) are probably the main responsible for the stability of the molecular form of this compound C1. The elongation of the hydrogen bond of the brominated cycle C1 compared to that of brominated coumarin C2 [12] (which has a donor-acceptor distance of 2.489 (6) Å) was explained by the mesomeric donor effect of the bromine atoms located in the aromatic cycle which could increase the electronic transfer. The stability of the structure was also ensured by intermolecular hydrogen bonds of O1–H2o1…O2i type between the phenolic group of cycle 1 and the ketone group of another cycle, through these bonds the molecules form parallel sheets along the axis [10] (Fig. 6) The geometric organization of the structure in the (101) plane can be described by the juxtaposition of the overlap-



**Fig. 5.** Part of the crystal stack showing the  $\pi$ - $\pi$  interactions between the benzene rings along the **A** axis.

ping molecules head-to-tail due to the centroid-centroid interactions between the benzene rings.

# 3.4. Hirshfeld surface analysis

Analysis of Hirshfeld surfaces (HS) suggest the possibility of obtaining additional insight into intermolecular interactions within crystals. The Hirshfeld area graphs of the title compound **C1** and the brominated coumarin **C2** [12] are shown in the Fig. 7, representing the areas, which have been mapped over  $d_{norm}$ , is scaled between [-0.321, 0.121] (Fig. 7(A) b) and [-0.130, 1.111] (Fig. 7(B) b), respectively and the shape index.



Fig. 6. Crystalline arrangement of C<sub>8</sub>H<sub>3</sub>O2Br<sub>5</sub> (C1), showing intermolecular interactions O-H ... O (in blue dotted line) along the axis [10].

The  $d_{norm}$  parameter was displayed as a surface with a redwhite-blue, where the red dots highlight the short contacts, the white areas represent the contacts around the van der Waals separation and the blue regions are devoid of close contacts [13].

The d<sub>norm</sub> mapping on HS of two compounds (Fig. 7(A) b, Fig. 7(B) b) shows a large visible circular depression (deep red spots) seen on the surface. These depressions plead for the interactions of hydrogen bonds (O-H... O) for both compounds. In addition, the close contacts of type Br...Br, Br...H-C and Br...C are present for compounds **C1** and **C2** by white areas on the d<sub>norm</sub> map. The shortest Br ... Br and C-H...Br interactions for compound **C1** reveal a distance of approximately 3.716 Å and 3.74 Å respectively (Fig. 7(A) a). The Br...Br interactions are also evidenced in shape index for the both compounds Fig. 6(A) c, Fig. 6(B) c by a red concave region around the acceptor brome atom and present a complementary blue convex region around the donor brome atom.

The shape index indicates the presence of the  $\pi$ - $\pi$  stack, which consist of red triangles (concave regions) and blue triangles (convex regions) for two compounds (marked by circles in red) [13]. The comparison of the shape index mapping between the brominated cycle **C1** and the brominated coumarin **C2** reveals that the new compound has weak  $\pi$ - $\pi$  stacking interactions. The 2D fingerprint traces confirm this deduction since the planar stack mainly corresponds to contacts C...C which appear as a tower like shape at the middle part of the fingerprint plot (Fig. 7). The analysis of the fingerprint graphs shows that the interaction C...C has a contribution to Hirshfeld surfaces of 4.2% for the brominated cycle **C1** and a very significant contribution of 12.5% for brominated coumarin **C2**.

The representations associated with 2D fingerprints have provided quantitative information on the crystal structure [46]. The contact enrichment ratios of the contacts were calculated in order to highlight the contacts [47] liable to cause the crystal structure were represented (Fig. 8).

The largest contribution to the overall crystal packing in the title compound **C1** is from the interactions Br...Br covered 40% of the total surface. On the other hand, the brominated coumarin **C2** reveals only 8.4% (Fig. 8c). In contrast, the interactions H...H show a very small contribution of 1.4% of the SH (**C1**) and an average contribution of 11.1% (**C2**). This significant contribution of Br...Br interactions to the total Hirshfeld surface is due to the fact that the majority of the molecular crystal surface is covered with Br atoms. The Br...H / H...Br interactions are represented by two peaks in the upper zone (Fig. 8e) with a contribution of 19% (**C1**) and 22.6% (**C2**).

The contacts 0...H / H...O have a significant contribution (Fig. 8b) for the brominated coumarin of 26.1% of SH compared to the brominated cycle 9.7% which manifests itself by important interactions due to the hydrogen bonds of O-H...O and C-H ... O. This type of interaction is manifested as two sharp points pointing to the lower left of the plot. The analysis of the 2D fingerprint plots for the title compound shows the existence of contacts type C...Br / Br...C (Fig. 7a) which are absent in the brominated coumarin crystal C2 with a significant contribution of 12.1% of SH and appears in the top middle of the plot in the form of characteristic wings. The proportion of 0...Br/Br...O interaction in the both compounds can also be gained by Hirshfeld surface analysis with a significant distribution in two-dimensional 12.4% (C1) and 12.8% (C2).



Fig. 7. The d<sub>norm</sub> (b) and shape index (c) Hirshfeld surfaces of C1: (A) and C2: (B), the dotted lines designate the close contacts between (Br...Br: blue color, Br...H: red color and Br...C green color).



Fig. 8. Two-dimensional fingerprint plots of the two compounds C1 and C2 showing percentages of contacts contributing to the total Hirshfeld surface area of the molecules: (a) all interactions, and delineated into (b) O···H/H···O, H/H, (c) Br···Br, (d) H···H, (e) Br···H and (f) C···C interactions.

### 3.5. Molecule structure

The optimized structure with the atom numbers and the selected geometric parameters have been given in Fig. 9 and Table 5, respectively.

Accordingly, the ring bond lengths C1-C2 and C3-C4 with having the sp<sup>2</sup> hybridization for the C1 molecule have been calculated at 1.38 Å and 1.43 Å, respectively. On the other hand, C3-C11 and C11-C12 bond lengths for the C1 molecule are predicted at 1.48 and 1.57 Å. Addition, the C4-O9, C11-O13, and C9-H10 bond lengths for the C1 molecule are calculated at 1.33, 1.22 and 0.98 Å, respectively. The C1-Br17 and C5-Br18 bond lengths for the ring of the C1 molecule have been predicted at 1.91 and 1.90 Å, whereas the other C-Br lengths for the C1 molecule have been calculated in 1.96–1.98 Å. As expected from the sp<sup>2</sup> hybridization of the central atoms, the C1-C2-C3 and C3-C4-C5 ring angles for the **C1** molecule have been calculated 120.7° and 118.6°; here, the hydroxyl group bonded to the C4 and Br18 atom connected to the C5 are responsible for the distortion (with 1.4°) from the planar 120°. Besides, the C12-C11-O13 angle for the C1 molecule has been calculated at 116.1° with a deviation of 3.9° from 120°. The C11-C12-Br14 and Br14-C12-Br15 angles related to the bromomethyl group are predicted at 109.4° and 108.1°, for the **C1** molecule. From Table 5, C1-C2-C3-C4, O9-C4-C5-Br18, C2-C3-C11-C12, and C4-C3-C11-O13 dihedral angles for the C1 molecule are calculated in 0.0° as the planar. Besides, the O13-C11-C12-Br15, C3-C11-C12-Br15, and C3-C11-C12-Br16 angles for the C1 molecule are determined at 118.7°, -61.3°, and 61.2°, respectively. For the C2 molecule, C1-C2-C3-C4, O14-C9-C12-C18, C9-C12-C18-O21 and O17-C13-C12-C18 torsion angles have been estimated as -0.0°, -0.6°, 2.8°, 1.2°; C2-C3-C4-C9 and C3-C4-C9-O14 dihedral angles are predicted in -179.7° with a small deviation from the planar angle. Also, the O16-C13-C12-C18 (-179.2°) and C13-C12-C18-O21 (-176.6°) dihedral angles for C2 molecule are deviated from the planar angle by -0.8° and -3.4°, respectively. The O21-C18-C19-Br22 and O21-C18-C19-Br23 dihedral angles for C2 molecule are calculated at 37.5° and -86.0°, orderly. It can be said that the observed and calculated optimized parameters for each compound are compatible with each other.

# 3.6. Frontier molecular orbital analysis

As known well, the FMO energies and appearances of them have long been used successfully to get a foresight of the behav-



Fig. 9. The optimized structures of C1 and C2 molecules at B3LYP/6-311++G(d,p) level.



Fig. 10. HOMO & LUMO (isoval:0.02) and MEP (isoval:0.0004) pilots of C1 and C2 molecules at B3LYP/6-11+G(d,p) level in the gas phase.

ior of both simple organic molecules [48–50] and complex systems [51–53], as they provide very useful information about the reactivity of the relevant chemical species. In Table 6, calculated chemical reactivity descriptors for C1, C2 molecules and their protonated forms B3LYP/6-311++G(d,p) level are presented as detailed. To explain stability, reactivity of molecules and to predict the directions of chemical reactions, in the literature some electronic structure principles known as Hard and Soft Acid-Base Principle (HSAB) [54], Maximum Hardness Principle [55], Minimum Polarizability Principle and Minimum Electrophilicity Principle are available in the literature [56]. In the book entitled "Conceptual Density Functional Theory and Its Application in the Chemical Domain" edited by Islam and Kaya [29], these electronic structure principles and their applications are presented as detailed. Chemical hardness is reported as the resistance towards electron cloud polarization or deformation of chemical species and according to Maximum Hardness Principle, hard molecules are more stable compared to soft ones. It is apparent from Table 6 that the hardest among studied molecules is C2 molecule. Minimum Polarizability Principle introduced with the help of Maximum Hardness Principle states that in a stable state polarizability ( $\alpha$ ) is minimized. Minimum Electrophilicity Principle [55,57] states that the natural direction of a chemical reaction is toward a state of minimum electrophilicity, namely the molecules with low electrophilicity values are more stable compared to others. It should be noted that both Minimum Polarizability and Minimum Polarizability Principle support that **C2** molecule is more stable than **C1** molecule. As to conclude all electronic structure principles indicate the stability of **C2** molecule.

Fig. 10 shows the HOMO, LUMO and MEP plots, which are commonly used to see the nucleophilic and electrophilic attack sites for the molecular systems. For the C1 molecule, it is seen that the HOMO, which implies the nucleophilic attack sites, is localized over the ring part and >C=O group, whereas the LUMO that is indicator of the electrophilic attack sites is localized over the whole molecule, except for the Br14 and Br17 atoms. For the C2 molecule, the HOMO density is over the rings and on Br23 atom, while the LUMO density is around the whole molecular surface except for the ketonic O17. On the other hand, the MEP plots have also provided information on the electron-rich and -poor regions of the molecular systems by using the color scale based on the electrostatic potential of the system; the red color implies the electronrich region for the nucleophilic attack and blue color shows the electron-poor region to electrophilic attacks. Accordingly, the red color for the C1 molecule is around the oxygen atoms, the blue color is around the C atoms bonded to the oxygen. H8 atom and two bromine atoms. As expected from the NBO results, the red color for the **C2** molecule is over both the ketonic groups whereas blue color is around the heteroatomic ring (Schema 1).



Schema 1. Synthesis of the brominated derivatives C1 and C2.

### 4. Conclusion

In this paper, we investigated bromo-derivatives prepared from the coumarin derivative "3-acetyl-4hydroxycoumarine". The obtained compounds "2, 2, 2-tribromo-1-(3,5-dibromo-2hydroxyphenyl) ethenone" (C1) and "3-(2,2-dibromoacetyl)-4hydroxy-2H-chromen-2-one" (C2) were characterized by spectroscopic techniques (IR, UV-vis), and their crystal structure was established by single-crystal X-ray structure determination. The optimized DFT geometries (B3PW91/6-311 G (2df, p)) and the spectral simulations of two derivatives compared agree well with the experimental data. Hirshfeld's analysis revealed the importance of Br  $\cdots$  Br (40%) and Br  $\cdots$  H / H  $\cdots$  Br (19%) of the total surface contacts in the molecular stack. The contacts  $\text{O}{\cdots}\text{H}$  /  $\text{H}{\cdots}\text{O}$  have a significant contribution for the brominated coumarin (C2) of 26.1% of SH compared to the brominated cycle(C1) 9.7%. The comparison of the shape index mapping between the brominated cycle C1 and the brominated coumarin C2 reveals that the new compound has weak  $\pi$ - $\pi$  stacking interactions. The analysis of the fingerprint graphs confirms this deduction since the planar stack mainly corresponds to contacts C...C which has a contribution to Hirshfeld surfaces of 4.2% for **C1** and a very significant contribution of 12.5% for C2. The frontier molecular orbital analysis revels that, for the **C1** molecule, it is seen that the HOMO is localized over the ring part and >C=0 group, whereas the LUMO is localized over the whole molecule, except for the Br14 and Br17 atoms. For the C2 molecule, the HOMO density is over the rings and on Br23 atom, while the LUMO density is around the whole molecular surface except for the ketonic O17. Both Minimum Polarizability and Minimum Polarizability Principle support that C2 molecule is more stable than **C1** molecule.

### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# **CRediT** authorship contribution statement

Ameni Brahmia: Conceptualization, Writing – original draft, Formal analysis, Writing – review & editing. Linda Bejaoui: Software, Writing – review & editing. Jan Rolicek: Software, Writing – review & editing. RachedBen Hassen: Methodology, Conceptualization, Writing – review & editing. Goncagül Serdaroğlu: Software, Writing – review & editing. Savaş Kaya: Software, Writing – review & editing.

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### Supplementary materials

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