Synthesis, X-ray structure, and DFT analysis of a binary complex of 3,3’-[(3-benzimidazolyl)methylene]bis(4-hydroxy-2H-1-benzopyran-2-one): 5-Methyl-1,3-thiazol-2(3H)-imine

Gopal Sharma 1, Anshul Uppal 1, Sumati Anthal 1, Madhukar Baburao Deshmukh 2, Priyanka Pandharinath Mohire 2, Tanaji Ramchandra Bhosale 2, Chellapanpillai Sudarsanakumar 3 and Rajni Kant 1.*

1 X-ray Crystallography Laboratory, Department of Physics, University of Jammu, Jammu Tawi, 180006, India
2 Department of Chemistry, Shivaji University, Kolhapur, 416004, India
3 School of Pure and Applied Physics, Mahatma Gandhi University, Kerala, 686560, India

c.sudarsan.mgu@gmail.com

ABSTRACT

A combined theoretical and experimental investigation on a pharmaceutically important binary complex 3,3’-[(3-benzimidazolyl)methylene]bis(4-hydroxy-2H-1-benzopyran-2-one): 5-methyl-1,3-thiazol-2(3H)-imine is presented in this manuscript. The compound crystallizes in the monoclinic crystal system with space group Cc with unit cell parameters: a = 19.8151(9) Å, b = 15.2804(6) Å, c = 8.3950(4) Å, β = 94.0990(10)°, V = 2535.36(19) Å³, Z = 4, 7 = 296(2) kg/mol = 0.184 mm⁻¹, Dcalc = 1.490 g/cm³, 35833 reflections measured (5.332° ≤ 2θ ≤ 56.678°), 6168 unique (Rint = 0.0467, R(f) = 0.0388) which were used in all calculations. The final R1 was 0.0435 (I > 2σ(I)) and wR2 was 0.1073 (all data). The crystal structure has been determined by the conventional X-ray diffraction method, solved by direct methods and refined by the full matrix least squares method. Intramolecular hydrogen bonding of the type N–H…O, C–H…N and O–H…N intermolecular interactions. The optimized structural parameters have been compared and the parameters like ionization potential, electron affinity, global hardness, electron chemical potential, electronegativity, and global electrophilicity based on HOMO and LUMO energy values were calculated at B3LYP/6-31G(d,p) level of theory for a better understanding of the structural properties of the binary complex.

1. Introduction

Coumarin derivatives, i.e., molecules containing the benzopyran-2-one or chromen-2-one ring system, are widely distributed throughout nature, occurring as secondary metabolites of plant species, notably in the tonka bean and Melilotus species [1]. Natural coumarins play an important role in plant biochemistry and physiology and act as antioxidants, enzyme inhibitors, and precursors of toxic substances [2]. These are also involved in the actions of plant growth hormones and growth regulators, the control over respiration and photosynthesis, as well as in the defense against various infections [3]. Substitutions on the benzopyrone ring influence the chemical structural [4], and biological properties of coumarins [5-7]. Coumarin heterocyclic derivatives exhibit diverse biological activities, as reviewed recently [8]. The biological activities of coumarin derivatives, in particular their therapeutic application as antifungal, antibacterial [9], antitubercular [10], antiacetylcholinesterase, anticanancer [11,12] anticoagulant, antimutagenic, anti-hepatitis C, anti-inflammatory [13], and analgesic [14] agents. Moreover, many coumarin derivatives are used as non-peptidic proteases [15], heat shock proteins [16,17], and monoamine oxidase [18]. The interest in coumarins has recently increased significantly because it was found that they inhibit HIV (human immune-deficiency virus), by affecting integrase and reverse transcriptase, which play a critical role in the replicative cycle of HIV [19-21].

Compounds containing a thiazole ring are known to have versatile pharmacological roles [22]. Substituted benzimidazoles also possess many biological activities, which is why benzimidazole derivatives are considered as an important moiety for the development of molecules of pharmaceutical interest [23,24].
With the aid of both coumarin and thiazole pharmaceuticals in mind, we were interested in developing a synthetic route to a binary complex that contains both entities with the aim of exploring whether or not the effects of the two units would work in concert in a pharmaceutical sense in the combined molecules [4,25].

The present study is focused on synthesis, X-ray structure, and DFT analysis of a binary complex of 3,3'-(3-benzimidazolyl)methylene]bis[4-hydroxy-2H-1-benzoypyran-2-one]:5-methyl-1,3-thiazol-2(3H)-imine. Studies on single crystal structure, crystal packing, molecular electrostatic potential map, and HOMO-LUMO plots provide supportive information about the crystal. The calculated optimized structural parameters were compared and the parameters like ionization potential, electron affinity, global hardness, electron chemical potential, electronegativity, and global electrophilicity based on HOMO and LUMO energy values were calculated at B3LYP/6-311G(d,p) level of theory for a better understanding of the structural properties.

2. Experimental

2.1. Materials and instrumentsation

All chemicals were purchased from Alfa Aesar and Spectrochem (PVT. Ltd, Mumbai, India), Sigma Aldrich and used without purification. The reaction was monitored by TLC. The desired structures of the synthesized compounds were confirmed by their relevant spectral data. The melting points were determined by the open glass capillary method and are uncorrected. The compounds were confirmed by IR and 1H NMR spectral data. The IR spectra were recorded on a JASCO FT-IR spectrophotometer (FTIR-4600) and the values are expressed uncorrected. The compounds were confirmed by IR and 1H NMR were determined by the open glass capillary method and are uncorrected. The compounds were confirmed by their relevant spectral data. The melting points were determined by the open glass capillary method and are uncorrected.

2.2. Synthesis of 3,3'-(3-benzimidazolyl)methylene]bis[4-hydroxy-2H-1-benzoypyran-2-one]:5-methyl-1,3-thiazol-2(3H)-imine

A mixture of 4-hydroxycoumarin (1 mmole) and dihydro benzimidazole 5-carbaldehyde (1 mmole), with 5 mL low transition temperature mixture was taken in a 50 mL round bottomed flask at room temperature to form the Knoevenagel condensation product, monitored by TLC and then 2-amino 5-methyl thiazole is added and the same reaction mixture refluxed for 20 min. The 2-amino 5-methyl thiazole is not involved in the Knoevenagel condensation, however, it forms a conglomerate with the chiral product formed by the condensation of two molecules of 4-hydroxy coumarin with 5-formyl dihydrobenzimidazole which separates in the form of transparent crystals. The progress of the reaction was monitored by TLC using petroleum ether:ethyl acetate (8:2, v/v). After the completion of the reaction, the mixture was cooled to room temperature and the product collected by simple filtration, washed with ethanol and diethyl ether. Finally, the crude product was recrystallized from ethanol to obtain the pure product. The Reaction scheme of the title compound is shown in Scheme 1.

2.3. Crystal structure determination and refinement

X-ray intensity data of the crystal of dimensions 0.25×0.30×0.35 mm³ were collected on a Bruker APEX-II CCD area detector diffractometer [26] equipped with graphite monochromated MoKa radiation (λ = 0.71073 Å). The data were collected at 296(2) K and 6168 reflections were found as unique. The intensities were measured by Φ+ω scan mode for θ range 2.67 to 27.46°. A total of 4717 reflections with I > 2σ(I) were treated as observed. Data was corrected for Lorentz-polarization and absorption factors. The structure was solved by direct methods using SHELXS [27] and was refined using SHELXL [28]. All non-hydrogen atoms of the binary complex were located from the best E-map. All hydrogen atoms were geometrically fixed (except N4 hydrogen atom) and allowed to ride on their parent carbon atoms with C-H = 0.93-0.97 Å, N-H = 0.86 Å. The final refinement cycles converged to an R-factor of 0.044 and wR(F2) = 0.107 for 4717 observed reflections. The residual electron density ranges from -0.32 to 0.28 e.Å⁻³. The geometry of the binary complex was calculated using the WinGX [29], PARST [30], and PLATON [31] software. Crystallographic information file (CIF) has been deposited at the Cambridge Crystallographic Data Centre with CCDC-1948179. A precise description of the crystallographic data of the X-ray structure is given in Table 1.

2.4. Theoretical calculation

The optimized structure of the compound 3,3'-(3-benzimidazolyl)methylene]bis[4-hydroxy-2H-1-benzoypyran-2-one]:5-methyl-1,3-thiazol-2(3H)-imine has been obtained by using Hartree-Fock (HF) method and is the same got re-optimized by using Becke’s three-parameter hybrid function (B3) [32,33] for the exchange part and the Lee-Yang-Parr (LYP) correlation function [34] using 6-311G basis set. The natural bond orbital (NBO) analyses, frontier molecular orbitals, atomic charges, and molecular electrostatic potential surface calculations were carried out by using Gaussian 09W [35] program.
3. Results and discussion

3.1. Single crystal structure analysis

The structure containing atom numbering scheme is shown in Figure 1 [36]. The bond distances, bond angles which play an important role in collating the structural properties of the binary complex with the related structures are presented in Table 2. The values of bond distance [37] and angles of all the rings are within the normal range. The C2-O1 = 1.213 Å and C26-O5 = 1.211 Å bond distances of the title compound are comparable with the values observed for some analogous structure [38,39]. In fact, the distances C9-O4 = 1.310 Å and C19-O3 = 1.295 Å are smaller than the values observed for some analogous structure [38,39]. The bond angles O1-C2-O2 = 114.7(3)°, O1-C2-C1 = 127.0(3)°, O5-C26-O6 = 114.0(3)° and O5-C26-C18 = 126.8(3)° are comparable with the values observed in some related structure. The atoms in the coumarin moiety deviate slightly from the planarity maximum deviation observed for C1 [-0.0342] and C23 [-0.0693] atoms. The imidazole ring in the molecule adopts an envelope conformation with a single mirror plane of symmetry passing through the C13-C14 bond (asymmetry parameter ΔC = 0.474).

The packing of the molecules in the unit cell is governed by both the intra and intermolecular interactions. In the crystal structure, adjacent molecules are interconnected through N1-H1···O1, N1-H1···O5, N4-H4A···O1, C23-H23···N2 and O3-H3A···N4 intermolecular hydrogen bonds. Here, the atoms O1, O5, N2, and N4 and nitrogen atom N1 of the five-membered thiazole ring act as hydrogen bond acceptors while the atoms N4, C23 and O3 act as hydrogen bond donors. In addition to the intermolecular hydrogen bonding network, C17-H17···O1, C17-H17···O5 and O4-H4C···O3 intramolecular interactions have also been observed which results in the formation of two (virtual five-membered rings) with a graph-set motif S(5) (Figure 1). The supramolecular assembly is formed by the intermolecular interactions of the type N-H···O and O-H…N which links the molecules to form a chain running parallel to a-axis, whereas hydrogen bond of the type C-H···N having atom C23 as the donor links the molecules to form a chain parallel to b-axis. The N1 atom of thiazole ring is the hydrogen bond donor that forms bifurcated hydrogen bonds with two different carbonyl groups [N1-H1···O1 (2.966 Å), N1-H1···O5 (2.724 Å)] give rise to R2(6) motif. Intermolecular hydrogen bonds of the type N-H···O and O-H…N are mainly responsible for stabilizing the crystal packing.

3. Results and discussion

Figure 1. ORTEP view of the binary complex with displacement ellipsoids drawn at 40% probability level.
Table 2. Comparison between experimental and calculated selected bond lengths (Å) and bond angles (°) of C$_{60}$H$_{50}$O$_{20}$C$_{6}$H$_{5}$N$_{5}$S using HF and DFT/6-311G basis set.

| Bond | Bond lengths | Experimental | Calculated | DFT/6-311G | Bond lengths | Experimental | Calculated | DFT/6-311G |
|------|--------------|--------------|------------|------------|--------------|--------------|------------|------------|
| C1-C3 | 1.387(5)     | 1.401        | 1.398      | C26-C28    | 1.211(4)     | 1.212        | 1.234      |
| C1-C4 | 1.387(5)     | 1.318        | 1.342      | C26-C26    | 1.211(4)     | 1.212        | 1.234      |
| C1-C7 | 1.533(4)     | 1.508        | 1.508      | C26-C29    | 1.295(4)     | 1.339        | 1.349      |
| N1-C2 | 1.425(5)     | 1.478        | 1.479      | C28-C28    | 1.366(4)     | 1.368        | 1.387      |
| C2-C2 | 1.375(4)     | 1.391        | 1.427      | C28-C27    | 1.317(6)     | 1.323        | 1.343      |
| C2-C3 | 1.213(4)     | 1.277        | 1.293      | C28-S1     | 1.755(4)     | 1.845        | 1.856      |
| C9-C10 | 1.526(5)    | 1.541        | 1.553      | C28-C29    | 1.500(6)     | 1.488        | 1.489      |
| C9-C11 | 1.310(4)    | 1.450        | 1.486      | C27-N1     | 1.373(6)     | 1.387        | 1.393      |
| C12-C13 | 1.527(5)   | 1.512        | 1.514      | C30-N1     | 1.326(5)     | 1.361        | 1.374      |
| C13-C14 | 1.367(6)   | 1.455        | 1.459      | C30-S1     | 1.717(4)     | 1.845        | 1.890      |
| N3-C16 | 1.369(4)    | 1.377        | 1.402      | C30-N4     | 1.317(5)     | 1.267        | 1.285      |
| N1-C17 | 1.418(6)    | 1.452        | 1.460      |           |              |              |            |

Table 3. Hydrogen bonding geometry (e.s.d.’s in parentheses).

| D-H-A (Å) | H-A (Å) | D-A (Å) | β D-H...A (°) |
|-----------|---------|---------|---------------|
| 0.82       | 1.67    | 2.462(3) | 162           |
| 0.98       | 2.33    | 2.871(4) | 114           |
| 0.98       | 2.33    | 2.826(4) | 110           |
| 0.86       | 2.27    | 2.966(4) | 138           |
| 0.86       | 2.12    | 2.724(5) | 127           |
| 0.83(5)    | 2.21(4) | 2.956(4) | 150(4)        |
| 0.93       | 2.58    | 3.468(5) | 160           |
| 0.82       | 2.26    | 2.839(4) | 128           |

Symmetry code: (i) 1/2 + x, 1/2 - y, -1/2 + z (ii) x, y, -1/2 + z (iii) x, y, z.

The molecular packing in the unit cell as viewed down the c-axis is shown in Figure 2 [36] and the geometry of intra- and inter-molecular hydrogen bonds is given in Table 3.

### 3.2. Theoretical calculation

#### 3.2.1. Molecular geometry

The optimized structure of 3,3’-[3-heximizidazolyl] maleimide)[bis(4-hydroxy-2H-1-benzopyran-2-one):5-methyl-1,3-thiazol-2(3H)-imine is shown in Figure 3. The optimized geometrical parameters (bond lengths and bond angles) calculated with HF and DFT methods using 6-311G basis set have been compared with the corresponding ones as obtained by X-ray diffraction method and are presented in Table 2.

#### 3.2.2. Molecular electrostatic potential (MEP)

The molecular electrostatic potential is a physically observable property that can be measured experimentally by diffraction approaches [40,41]. It is also used to illustrate the wide-raying electronic and nuclear charge distribution, which is an appropriate feature for understanding the reactivity of various species [42]. The potential, V(r), is typically written in terms of atomic units (a.u) and has the following form [43].
Figure 3. Optimized structure of 3,3'-(3-benzimidazolyl)methylene][bis(4-hydroxy-2H-1-benzopyran-2-one):5-methyl-1,3-thiazol-2(3H)-imine.

Figure 4. Molecular electrostatic potential map of 3,3'-(3-benzimidazolyl)methylene][bis(4-hydroxy-2H-1-benzopyran-2-one):5-methyl-1,3-thiazol-2(3H)-imine.

\[ V(r) = \sum_{A} \frac{Z_A}{|R_A - r|} - \int \frac{\rho(r')}{|r - r'|} d^3 r' \]  (1)

where \( Z_A \) is the charge of the nucleus \( A \) located at \( R_A \), \( \rho(r') \) is the electronic density function of the molecule, and \( r' \) is the dummy integration variable.

MEP has been constructed using DFT/6-311G level of theory for 3, 3'-[(3-benzimidazolyl)methylene] bis(4-hydroxy-2H-1-benzopyran-2-one): 5-methyl-1, 3-thiazol-2(3H)-imine and is shown in Figure 4. In the color scheme of MEPs, red represents the electron rich, partially negative charge which is the preferred site for electrophilic attack, blue corresponds to electron deficient, partially positive charge which is the preferred site for nucleophilic attack, yellow for slightly electron rich region; green for neutral respectively. The color code of 3,3'-[(3-benzimidazolyl)methylene] bis(4-hydroxy-2H-1-benzopyran-2-one): 5-methyl-1,3-thiazol-2(3H)-imine is in the range between \(-9.703 \times 10^{-2}\) (deepest red) to \(9.703 \times 10^{-2}\) (deepest blue). It can be seen that the negative regions are mainly over the oxygen atoms and the positive potential sites are around the hydrogen atoms.

3.2.3. HOMO-LUMO analysis

The highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are known as frontier molecular orbitals (FMOs). The FMOs plays an important role in the optical and electrical properties as well as in quantum chemistry [44]. The HOMO represents electron-donating ability, while LUMO represents the electron accepting ability [45]. The pictorial representation of the energies of molecular orbitals is shown in Figure 5, the positive phase is represented by the red color and negative phase represented in green color). The HOMO lies at \(-4.82\) eV and spreads over the thiazole ring whereas the LUMO is located at \(-3.36\) eV which shows that the charge transfer to imidazole ring within the molecule and the energy gap is \(1.46\) eV. The energy difference between the HOMO and the LUMO orbital is called as energy gap that is important for the stability of structures. Both the HOMO and LUMO orbitals help describe the chemical reactivity and kinetic stability of the binary complex. By using HOMO and LUMO energy values for a molecule, the electronegativity and chemical hardness can be calculated as follows [46]:

\[ \chi = -\frac{E_{\text{HOMO}} + E_{\text{LUMO}}}{2} = 4.09 \]  (2)

\[ \eta = \frac{E_{\text{LUMO}} - E_{\text{HOMO}}}{2} = 0.73 \]  (3)

\[ S = \frac{1}{2}\eta = 0.68 \]  (4)

\[ l = -E_{\text{HOMO}} = 4.82 \]  (5)

\[ A = -E_{\text{LUMO}} = 3.36 \]  (6)
Global Electrophilicity (ω) Global hardness (η) Electronegativity (χ) Electron affinity (A) Ionization potential (I)

Molecular parameters (eV) Mulliken [47] methods using HF/6-311G and B3LYP/6-311G

For each donor NBO (i) and acceptor NBO (j), the stabilization energy $E(2)$ associated with electron delocalization between donor and acceptor is estimated as

$$E(2) = \Delta E_{ij} = q_i F_{ij}^2 / E_i - E_j$$

where $q_i$ is the donor orbital occupancy, $E_i, E_j$ are diagonal elements (orbital energies), and $F_{ij}$ is the off-diagonal NBO Fock matrix element.

Larger the $E(2)$ value, the more intensive is the interaction between the electron donor and electron acceptor, i.e., the more donating tendency from the electron donor to electron acceptors and the extent of electron delocalization is greater. The results of second-order perturbation theory analysis of Fock matrix at B3LYP/6-311G level of theory are collected in Table 6.

In this compound, the strong intra-molecular hyperconjugation interaction of the $\pi$ electrons from C18-C19 to the $\pi^*$ antibonding orbitals of C26-O5 and $\sigma^*$ (C6-C5) to the $\sigma^*$ antibonding orbital C8-C7 leads to the stabilization energy of 30.36 and 23.44 kJ/mol, respectively. The most important interaction energy related to the resonance in the binary complex is the electron donating from the lone pair LP O1 atom to $\pi$ (C1-C2) and LP N3 atom to $\sigma^*$ (C13-C12) which leads to a stabilization energy of 56.98 and 39.65 kJ/mol, respectively.

Table 4. HOMO-LUMO and other related molecular properties of 3,3’-[[(3-benzimidazolyl)methylene]bis(4-hydroxy-2H-1-benzopyran-2-one):5-methyl-1,3-thiazol-2(3H)-imine.

| Molecular parameters (eV) | B3LYP/6-311G |
|--------------------------|--------------|
| HOMO                     | -3.36        |
| LUMO                     | -4.82        |
| Ionization potential (I) | 3.36         |
| Electron affinity (A)    | 4.09         |
| Electronegativity (χ)    | 0.73         |
| Global hardness (η)      | -0.09        |
| Chemical potential (µ)   | 2.04         |

Figure 5. HOMO-LUMO plot of 3,3’-[(3-benzimidazolyl)methylene]bis(4-hydroxy-2H-1-benzopyran-2-one):5-methyl-1,3-thiazol-2(3H)-imine.
Table 5. Mulliken charges using HF and DFT theory.

| Atom no | Mulliken (HF/6-311G) | Mulliken (B3LYP/6-311G) |
|---------|----------------------|------------------------|
| C13     | 0.251087             | 0.314476               |
| C14     | 0.485303             | 0.258599               |
| C15     | -0.039555            | 0.049746               |
| C10     | 0.287460             | 0.103562               |
| C11     | -0.438188            | -0.320469              |
| C12     | 0.110025             | 0.053939               |
| H15     | 0.225850             | 0.211357               |
| H12     | 0.215910             | 0.190972               |
| N3      | -0.946875            | -0.820857              |
| N2      | -0.964970            | -0.774947              |
| C16     | 0.182368             | 0.069975               |
| H3      | 0.361921             | 0.348392               |
| H2      | 0.399899             | 0.368059               |
| H16B    | 0.210958             | 0.217518               |
| H16A    | 0.208974             | 0.220085               |
| C17     | -0.493542            | -0.480255              |
| C1      | 0.084671             | 0.018405               |
| C2      | 0.020503             | 0.503461               |
| C9      | 0.094619             | -0.071655              |
| C8      | 0.021775             | 0.037947               |
| C3      | 0.350507             | 0.236978               |
| H11     | 0.297138             | 0.268804               |
| O2      | -0.789026            | -0.616687              |
| O1      | -0.797180            | -0.596030              |
| O4      | -0.738375            | -0.591135              |
| H4C     | 0.408051             | 0.368489               |
| C7      | -0.149051            | 0.113087               |
| C6      | -0.175219            | -0.157784              |
| C5      | -0.157243            | -0.151340              |
| C4      | -0.182099            | -0.162701              |
| H7      | 0.178553             | 0.161375               |
| H6      | 0.161152             | 0.147715               |
| H5      | 0.164646             | 0.149822               |
| H4      | 0.289050             | 0.249553               |
| C18     | -0.233884            | -0.105957              |
| C26     | 0.743513             | 0.496077               |
| C19     | 0.616685             | 0.388383               |
| C20     | -0.213317            | -0.156950              |
| C25     | 0.387685             | 0.289643               |
| O6      | -0.687697            | -0.509396              |
| H17     | 0.309773             | 0.265387               |
| O5      | -0.514493            | -0.371347              |
| C21     | -0.079446            | -0.068824              |
| C22     | -0.187771            | -0.165099              |
| C24     | -0.191184            | -0.163029              |
| C23     | -0.183081            | -0.119996              |
| H21     | 0.213159             | 0.183199               |
| H22     | 0.169470             | 0.152324               |
| H23     | 0.170681             | 0.154871               |
| H24     | 0.201202             | 0.180110               |
| O3      | -0.819505            | -0.633236              |
| H3A     | 0.480926             | 0.398229               |
| C28     | -0.409296            | -0.380254              |
| C27     | 0.382935             | 0.317406               |
| C30     | 0.368787             | 0.216696               |
| N1      | -0.066889            | -0.704579              |
| S1      | 0.192235             | 0.200104               |
| C29     | -0.568555            | -0.595302              |
| N4      | -0.670799            | -0.546805              |
| H29C    | 0.187736             | 0.192695               |
| H29A    | 0.188584             | 0.192440               |
| H29B    | 0.190970             | 0.196152               |
| H4A     | 0.264622             | 0.254694               |
| H1      | 0.485942             | 0.432944               |
| H27     | 0.259014             | 0.226059               |

### 3.2.6. Fukui function

Density Functional Theory is a powerful tool for the study of reactivity and selectivity in a molecule [50]. The most basic and commonly used local reactivity parameter is the Fukui function, which indicates the tendency of the electron density to deform at a given position upon accepting or donating electrons [51,52]. Fukui function gives us information about the electrophilic/nucleophilic power of a given atomic site in a molecule. The condensed Fukui functions on the jth atom site can be expressed as:

\[ f_i^+ = q_i(N + 1) - q_i(N) \]  \hspace{1cm} (8)

\[ f_i^- = \frac{1}{2} [q_i(N + 1) - q_i(N - 1)] \]  \hspace{1cm} (9)

\[ f_i^- = q_i(N) - q_i(N - 1) \]  \hspace{1cm} (10)

where \( f_i^- \) for nucleophilic attack, \( f_i^+ \) for electrophilic attack and \( f_i^0 \) for free radical. In these equations, \( q_i \) is the atomic charge at the jth atomic site in the neutral (N), anionic (N+1), or cationic (N-1) chemical species.
The atomic charges either calculated by natural population analysis (NPA) or by Mulliken population analysis (MPA) have been used to calculate the Fukui function. In the present study the values of Fukui Function calculated from the NBO charges. The dual descriptor $\Delta f(r)$ [53] for the calculation of nucleophilicity and electrophilicity is defined as the difference between the nucleophilic and electrophilic Fukui functions and is given by the Equation (11):

$$\Delta f(r) = f^+ - f^-$$  \hspace{1cm} (11)

If $\Delta f(r) > 0$, then the site is favored for nucleophilic attack, whereas if $\Delta f(r) < 0$, then the site is favored for an electrophilic attack. According to the dual descriptor, $\Delta f(r)$ gives a transparent distinction between nucleophilic and electrophilic attacks at a particular site with their sign. From the values reported in Table 7, according to the condition for dual descriptor, nucleophilic site in our title molecule is C13, C13, C15, C1, O1, O3, O4, O5, N1, N4, S1, H1 and H1 are positive values (i.e. $\Delta f(r) > 0$). Similarly, the electrophilic site is C10, C12, C14, C2, C3, C9, C19, C26, C17, N2, N3, O2, O6, H2, H3, H12 and H15 negative values (i.e. $\Delta f(r) < 0$).

### 4. Conclusion

In the present investigation, the synthesis and the molecular structure analysis of 3,3′-[(3-benzimidazolyl)methylene]bis[4-hydroxy-2H-1-benzopyran-2-one]-5-methyl-1,3-thiazol-2(3H)-imine has been reported by X-ray crystallographic techniques and NBO, HOMO-LUMO, Fukui function, atomic net charge analysis by HF and DFT-B3LYP methods at 6-311G basis set. In the crystal structure, the presence of coumarine and 5-methyl-1,3-thiazol-2(3H)-imine promotes the formation of a transparent distinction between nucleophilic and electrophilic attacks at a particular site with their sign.
intermolecular hydrogen bond network. The molecular packing in the unit cell is stabilized via N-H⋯O and C-H⋯N intermolecular interactions. The computed geometric parameters (bond length, bond angle) have been compared with their corresponding experimental data. The molecular electrostatic potential map indicates that the negative potential sites are on electronegative atoms and the positive potential sites are around the hydrogen atoms. These sites provide information concerning the region from where the structure may result into the formation of intra- and intermolecular interactions.

Acknowledgements
Rajni Kant acknowledges the Research Grants as sanctioned under Rashtriya Uchchatar Shiksha Abhiyan (RUSA) 2.0 Project (Ref: No: RUSA/JU/2/2019-20/111/3588-3636).

Supporting information
CCDC-1948179 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

Disclosure statement
Conflict of interest: The authors declare that they have no conflict of interest.

Conflict of interest: The authors declare that they have no conflict of interest.

ORCID
Gopal Sharma http://orcid.org/0000-0003-4780-2804
Anshul Uppal http://orcid.org/0000-0001-8203-616X
Sumati Anthal http://orcid.org/0000-0001-7947-7335
Madhukar Baburao Deshmukh http://orcid.org/0000-0001-7097-2356
Priyanka Pandharinath Mohire http://orcid.org/0000-0003-4644-1111
Tanaji Ramchandra Bhosale http://orcid.org/0000-0002-0372-7702
Che Ilappanpillai Sudarsanakumar http://orcid.org/0000-0003-2750-7795
Rajni Kant http://orcid.org/0000-0001-8043-2329

References
[1] Kontogiorgis, C.; Detsi, A.; Hadjipavlou-Litina, D. Exp. Opin. Therap. Pat. 2012, 22, 437-454.
[2] Kostova, I. Curr. Med. Chem. Anti-Cancer Agents 2005, 5, 29-46.
[3] Weitmann, I. Gomourian: Biology, Applications and Mode of Action, John Wiley & Sons, USA, 1997, pp. 1-22.
[4] Saeed, A.; Ashraf, S.; Florke, U.; Delgado Espinoza, Z. Y.; Erben, M. F.; Weinmann, I. Coumarins: Biology, Applications and Mode of Action, 2012, 83-107.
[5] Saeed, A.; Zaib, S.; Ashraf, S.; Iftikhar, J.; Muddassar, M.; Zhang, K. Y.; Ishbal, J. Bioorg. Chem. 2015, 63, 58-63.
[6] Medina, F. G.; Marrero, J. G.; Macias-Alonso, M.; Gonzalez, M. C.; Cordova-Guerrero, J.; Teissier Garcia, A. G.; Oseguera-Robles, S. Nat. Prod. Rep. 2015, 32, 1472-1507.
[7] Stryer, T.; Ramachandran, V. N.; Smyth, W. F. Int. J. Antimicrob. Agents 2009, 33, 421-426.
[8] Manvar, A.; Malde, A.; Verma, J.; Virodila, V.; Mishra, A.; Upadhyay, K.; Acharya, H.; Coutinho, E.; Shah, A. Eur. J. Med. Chem. 2008, 43, 2395-2403.
[9] Bellotti, F.; Fontana, G.; Dal Bo, L.; Careani, N.; Giommiarelli, C.; Zunino, F. Bioorg. Med. Chem. 2010, 18, 3543-3550.
[10] Yu, S.; Suzuki, M.; Xie, L.; Morris-Natschke, S. L.; Lee, H. K. Med. Rev. 2003, 23, 322-345.
[11] Kalkihmbrik, G. R.; Kulkami, G. M.; Kamanavalli, C. M.; Premkumar, N.; Audas, S. M. B.; Sun, C. M. Eur. J. Med. Chem. 2008, 43, 2178-2188.
[12] Keri, S. R.; Hosamani, K. M.; Shingalgarap, R. V.; Hug, M. H. Eur. J. Med. Chem. 2010, 45, 2597-2605.
[13] Wood, W. J.; Patterson, A. W.; Tsuonouka, H.; Jain, R. K.; Ellman, J. A. J. Am. Chem. Soc. 2005, 127, 1525-1527.
[14] Shashidhara, K.; Kumar, A. S.; Sarkar, J.; Sinha, S.; Bioorg. Med. Chem. Lett. 2010, 20, 7205-7211.
[15] Radani, C.; Le Bras, G. I.; Messandou, S.; Bouclier, C. I.; Peyrat, J. F. O.; Brion, J. D.; Marsaud, V. r.; Renoir, J. M.; Allani, M. d.; Bioorg. Med. Chem. Lett. 2008, 18, 2429-2434.
[16] Chimenti, F.; Secci, D.; Bolosac, A.; Chimenti, P.; Grasene, A.; Belealni, O.; Turini, P.; Alcaro, S.; Ortuso, F. Bioorg. Med. Chem. Lett. 2004, 14, 3679-3703.
[17] Nolan, A. K.; Doncaster, R. J.; Dunstan, S. M.; Scott, A. K.; Frenkel, D.; Siegel, D.; Ross, D.; Barnes, J.; Levy, C.; Leys D. J. Med. Chem. 2009, 57, 7142-7156.
[18] Mahajan, D. H.; Panneconceco, C.; De Clercq, E.; Khialdha, K. A. Arch. Pharm. 2009, 342, 281-290.
[19] Zhao, H.; Neamati, N.; Hong, H.; Mazumder, A.; Wang, S.; Sunder, S.; Milne, G. W. A.; Pommier, Y.; Burke, T. R. J. Med. Chem. 1997, 40, 242-249.
[20] Saeed, A.; Arif, M.; Erben, M. F.; Florke, U.; Simpson, J. Spectrochim. Acta A 2018, 198, 290-296.
[21] Lee, Y.; Yao, J.; Yang, L.; Peng, C.; Tang, W.; Wang, G.; Zuo, J.; Lu. W. Arch. Pharm. Chem. Life Sci. 2011, 2, 78-83.
[22] Arjmand, F.; Aziz, M. Eur. J. Med. Chem. 2009, 44, 834-844.
[23] Osman, H.; Arshad, A.; Lam, C. K.; Bagley, M. C. Chem. Cent. J. 2012, 6, 32-42.
[24] Brueder (2009). SADABS. Bruker AXS Inc, Madison, Wisconsin, USA.
[25] Sheildrick, G. M. Acta Cryst. A 2008, 64, 112-122.
[26] Sheildrick, G. M. Acta Cryst. C 2015, 71, 3-8.
[27] Farrugia, L. J. Appl. Cryst. 2012, 45, 849-854.
[28] Nardelli, M. J. Appl. Crytal. 199. 20, 659-659.
[29] Spek, A. L. Acta Cryst. D 2005, 69, 148-155.
[30] Becke, A. D. Chem. Phys. 1993, 98, 5640-5652.
[31] Becke, A. D. Phys. Rev. A 1988, 39, 3098-3110.
[32] Lee, C. T.; Yang, W. T.; Parr, R. G. Phys. Rev. B 1988, 37, 785-789.
[33] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Peng, J. Y.; Wasserman, S. T.; Farkas, O.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Robb, M. A.; Vreven, T.; Throssell, K.;赞, K. Y.; Ishbal, J. Bioorg. Chem. 2015, 63, 58-63.
[46]. Pearson, R. G. Proceed. Nat. Acad. Sci. USA 1986, 83, 8440-8441.
[47]. Mulliken, R. S. J. Chem. Phys. 1955, 23, 1833-1840.
[48]. Choo, J.; Kim, S.; Joo, H.; Kwon, Y. J. Mol. Struct. 2002, 587, 1-8.
[49]. Reed, A. E.; Curtiss, L. A.; Weinhold, F. Chem. Rev. 1988, 88, 899-926.
[50]. Parr, R. G.; Yang, W. Density Functional Theory of Atoms and Molecules, Oxford University Press, New York, 1989.
[51]. Ayers, P. W.; Parr, R. G. J. Am. Chem. Soc. 2000, 122, 2010-2018.
[52]. Parr, R. G.; Yang, W. J. Am. Chem. Soc. 1984, 106, 511-516.
[53]. Morell, C.; Grand, A.; Torre-Labbe, A. J. Phys. Chem. 2005, 109, 205-212.