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A Rapid Ultrasound Synthesis of Xanthenediones Catalyzed by Boric acid in Ethanol-Water Medium: Single Crystal, DFT and Hirshfeld Surface Analysis of Two Representative Compounds



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ABSTRACT

A highly versatile and efficient ultrasound promoted synthesis of xanthenedione derivatives is achieved through condensation of dimedone with various aromatic aldehydes using boric acid as catalyst in ethanol-water medium. The advantages of this method being, mild reaction conditions, short reaction time, easy work-up, purification of products by non-chromatographic methods and additionally this method provides excellent yields. Two of the Xanthendiones derivatives 3a and 3b gave good crystals on recrystallization and their molecular structures were confirmed by crystallographic studies. The molecules in the crystal lattice are held together by weak intermolecular C-H•••O and C-H•••N interactions. Further insights into these interactions using Hirshfeld surface analysis and DFT/B3LYP studies show that in compound **3a** H•••H (54.7%), O•••H (18.3%) and in **3b** H•••H (53.7%), O•••H (17.6%) are the major contributors to the intermolecular interactions which stabilize the crystal structures. In order to determine molecular electrical transport properties, we studied the energy difference between Highest Occupied, HOMO, and Lowest Unoccupied, LUMO orbitals and the HOMO and LUMO energy gap for compounds 3a and 3b was found to be 3.9261 eV and 4.6436 eV respectively. The 2D fingerprint plot provided percentage contribution of each individual atom-to-atom interactions. The Mulliken atomic charges and molecular electrostatic potential on molecular van der Waals surface were calculated to know the electrophilic and nucleophilic regions of the molecular surface.

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1. Introduction

Design and development of an accessible procedure for the synthesis of simple heterocycles with various functionalities is a worthwhile contribution in organic synthesis. Xanthendiones are important structural units in heterocyclic class of compounds which have been widely investigated in recent years. In particular, the xanthenedione moiety is present in several natural products [1] and they are also valuable synthons because of the inherent reactivity of their pyran ring [2]. Synthesis of xanthenedione derivatives has been of considerable interest to chemists, due to their wide application in medicine and pharmaceutics such as antiviral [3], antibacterial agents [4], photosensitizers for photodynamic therapy, antagonists of zoxazolamine [4,5], and anti-inflammatory drugs [6]. Furthermore, xanthenes are also reported as staining

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dyes [7,8], fluorescent probes for the visualization of biomolecules [9], laser dyes [10] and corrosion inhibitors [11].

A large number of organic reactions that have been carried out under ultrasonic irradiation require short reaction time and involves easier work-up procedures than conventional methods and above all are known to give higher yields [12]. Ultrasound provides an unusual mechanism for generating high-energy chemistry. Ultrasound works on the phenomenon of cavitation; which involves the growth, oscillation, and collapse of bubbles under the action of an acoustic field.

Owing to their unique biological profile, numerous methodologies have been developed for the synthesis of xanthenediones. Many such catalysts, for example are InCl₃.4H₂O [13], NaHSO₄•SiO₂ [14], silica sulfuric acid [15], TiO₂/SO₄²⁻ [16], ZrOCl₂•8H₂O [17], FeCl₃•6H₂O [18], Dowex-50W [19], Fe³⁺-montmorillonite [20], amberlyst-15 [21] and alumina sulfuric acid [22] as solid acid catalysts. In addition, the synthesis of other xanthenedione derivatives, catalyzed by a Preyssler-type heteropoly acid [23], HPA/SiO2 [24] and HPWA/ MCM-41 [25] have also been reported.



Scheme 1. Syntheses of xanthenediones using boric acid in ultrasound condition.

However, many of the reported protocols are, although efficient, a few of them suffer from serious drawbacks such as tedious preparation of the catalyst, high reaction temperature, longer reaction time, low yields, excess use of reagents as well as toxicity of catalysts or cost of catalysts. Among the numerous methods for the synthesis of xanthenediones, the condensation of aldehydes with active methylene compound like dimedone in the presence of boric acid as a catalyst is found to be very efficient. In recent years, boric acid has gained special attention as catalyst in organic synthesis because of its many advantages associated with this acid, such as excellent solubility in water, uncomplicated handling, inexpensiveness and eco-friendly nature.

In pursuit of our work to develop environmentally friendly synthetic methodologies for the synthesis of xanthenediones, the present work is envisioned as the green chemistry approach using water-ethanol solvent system for ultrasound mediated domino reaction in efficient synthesis of xanthenediones. To the best of our knowledge, boric acid (BO₃H₃ or B (OH)₃) has not been used as a catalyst for the synthesis of xanthendiones and has attracted our attention to investigate the application of boric acid as a catalyst. The environmental impact is reduced by the fact that all reactions are carried out in water-ethanol system and are ultrasound mediated reactions which has easy work up, a greener solvent, shorter reaction time and hence a complete green approach.

2. Materials and instruments

All reactions were performed in oven dried apparatus. All the chemicals were purchased from Sigma-Aldrich and Spectrochem-India. Reactions were monitored on Merck F-254 pre-coated TLC plastic sheets using hexane as mobile phase. Melting points were determined by the open capillary method using Guna melting point apparatus and remain uncorrected. IR spectra were recorded on a Shimadzu FT-IR 8400S spectrometer and the values are reported in wave number (cm⁻¹). ¹H NMR and ¹³C NMR were obtained on a Bruker AMX 400 spectrometer using CDCl₃ with tetramethylsilane as internal standard. Mass spectra were recorded on Finnigan MAT (Model MAT8200) spectrometer. Ultrasonication was performed using SIDILU, sonic bath working at a constant frequency of 35 kHz and an output power of 70W at 26[°]C (maintained by circulating water). The reactions were performed in open vessels without any mechanical stirring.

3. Experimental

3.1. General procedure for synthesis of xanthendiones

A mixture of various aromatic aldehydes (1 mmol), dimedone (2 mmol), and catalytic amount of boric acid was added in a round bottom flask with a 1:1 mixture of ethanol-water solvent system and placed in a sonic bath and sonicated at room temperature until the reaction was complete Scheme 1. Reactions were monitored

by thin-layer chromatography (TLC) and after completion of the reaction, the mixture was cooled to room temperature and filtered. The precipitate obtained was washed with water. The crude product was further recrystallized using ethanol as the solvent.

4. Investigation techniques

4.1. X-ray single crystal structural analysis

The X-ray diffraction data, for the compounds **3a** and **3b** were collected on a Bruker Smart CCD Area Detector System using MoK α (0.71073 Å) radiation in $\omega - \phi$ scan mode. The data were reduced using SAINT-Plus [26]. The structure in each case was solved by Direct Methods and refined on F² using SHELX-97 [27] package. All the non-hydrogen atoms were refined anisotropically. As the hydrogens were not readily revealed from difference Fourier maps, they were included in the ideal positions with fixed isotropic U values and they were riding with their respective non-hydrogen atoms. The difference Fourier map, after the refinement, was essentially featureless in all cases. The mean plane calculations were done using the program PARST [28]. Diagrams and publication material were generated using ORTEP-3 [29] and PLATON [30].

4.2. Computational details

Compound **3a** and **3b** were theoretically explored in detail for the comparative investigation with experimentally obtained results of X-ray diffraction. All calculations were performed by Gaussian 16 software package [31] and were visualized using GaussView 6 without any constraints on the geometry [32]. Density Functional Theory (DFT) calculations were performed using B3LYP functional proposed by Becke [33-34] and Lee, Yang, Parr with all electron pople 6-311+G (d,p) basis set [35-36] as implemented in the Gaussian 16 package. All the structure were optimized without any constraints. The structure has been characterised as minima on potential energy surface (PES) by performing harmonic vibration analysis. The molecular orbital energies were calculated using the 6-311+G (d,p) basis set. No symmetry constraints were applied and only the default convergence criteria were used during the geometric optimizations. In addition to this, Molecular electrostatic potential map (MEP) was obtained from the output of B3LYP/6-311+G (d,p) basis set.

5. Results and Discussions

5.1. Chemistry of Xanthenediones

We initiated our investigation by carrying out a comparative study between the conventional reflux method versus sonication technique. The study was attempted by using a model reaction between 4-hydroxy benzaldehyde and dimedone in presence boric acid as catalyst at 60°C under reflux condition and a similar reaction in sonicator maintained at 26°C. Once the reactions were

Table 1	
Effect of catalyst on sonication reaction.	
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Trial No.	Reaction carried out by sonication at 26°C.	Duration (mins)	%Yield obtained
1.	Reaction carried out in absence of catalyst	170	60
2.	Reaction catalysed by conc. HCl	130	73
3.	Reaction catalysed by boric acid	50	95(3c)

Table 2

Optimisation of solvent for the synthesis of Xanthenedione derivatives in ultrasound conditions.

Entry	Solvent	Time(mins)	Yield (%) ^a
1.	CH₃CN	130	76
2.	CHCl ₃	115	76
3.	CH ₂ Cl ₂	90	85
4.	Water	80	75
5.	C ₂ H ₅ OH	75	85
6.	C ₂ H ₅ OH- Water	50	95

*a Yields refer to pure isolated product

completed it was observed that the reaction carried out in reflux condition had a serious drawback over the sonicated reaction mixture in terms of its reaction duration, purity and in product vield. Reflux reaction was carried out at 60°C which gives a vield of 74% in 7-8 hours, whereas the reaction carried out by sonicator at 26°C was almost completed within 50 minutes with a yield of 95%. Therefore, we opted for sonication technique at 26°C in ethanol. Further, in order to study the importance of boric acid as the catalyst we conducted a model reaction between 4-hydroxy benzaldehyde and dimedone at 26°C in one-pot using two different types of catalyst simultaneously at the same time. Initially, the reaction (Table 1, trial 1) was carried out in absence of the catalyst and the reaction was found to go to completion after a longer duration of 170 mins with much lesser yield of 60%. In trial 2 we carried out the same reaction with catalytic amount of concentrated hydrochloric acid and in trial 3 the reaction was carried out in presence of boric acid as the catalyst, both the reactions were sonicated in ethanol. Once the reaction was completed the yield of the product was found to be more in case of boric acid along with less by-products, easy eco-friendly workup with water, less tedious process and the product was formed in shorter duration when compared with conc. HCl. (Table 1) The desired product was isolated as a white crystalline solid in 95% yield after 50 mins. Hence, considering the advantages of boric acid as the catalyst in sonication, the first of its kind method has been reported here. Later the same reaction was optimised with different solvents and highest yields were obtained in waterethanol system. (Table 2) Hence, we carried out all the reactions under the same reaction conditions that afforded the desired products in higher yields with different substituents (Table 3). Interestingly, the aryl aldehydes containing either electron-withdrawing or electron-donating substituents reacted smoothly and provided the desired products in good to excellent yields. High yields were obtained when the reaction was carried out with electron-donating groups such as *p*-hydroxybenzaldehyde, *p*-methoxybenzaldehyde, p-chlorobenzaldehyde and p-bromobenzaldehyde. (3c, 3h, 3d and 3f) However, electron-withdrawing substituents afforded moderate yields when reaction was carried out with *m*-cyanobenzaldehyde and *p*-cyanobenzaldehyde. (3a and 3b) (Table 3) A plausible mechanism for the synthesis xanthenedione is shown below (Fig. 1) with boric acid as the bronsted acid catalyst. Initially activation of substituted benzaldehyde (1) takes place with boric acid followed by attack of enol form of dimedone (2) to give intermediate (3) by loss of water molecule through Clasien-condensation mechanism. Later the second molecule of dimedone undergoes Micheal addition with intermediate (**3**) further, the condensed intermediate furnishes the products **3a–j** by the loss of water molecule.

5.2. Crystallographic Studies

5.2.1. Compound (**3a**)

Intensity data were collected at 298 K in the ω - ϕ scan mode. A total of 19545 reflections were collected, resulting in 5497 [R (int) = 0.0653] independent reflections, of which the number of reflections satisfying I > 2σ (I) criteria were 5497. The R factor for observed data finally converged to R1 = 0.0638.

5.2.2. Compound (**3b**)

Intensity data were collected at 293 K in the ω - ϕ scan mode. A total of 17535 reflections were collected, resulting in 4044 [R (int) = 0.0289] independent reflections, of which the number of reflections satisfying I > 2σ (I) criteria were 4044. The R factor for observed data finally converged to R1 = 0.0446.

The ORTEP view of the molecules **3a** and **3b** with atom labelling is shown in Fig. 2. Packing of molecules for compound **3a** and **3b** is shown in Fig. 3 and 4. Summary of crystallographic data and other structure refinement parameters of the compounds **3a** and **3b** are given in Table 4. Table 5 gives the other weak interaction parameters in compound **3a** and Table 6 gives weak interaction parameters for compound **3b**.

Compounds **3a** and **3b** crystallize in the triclinic and orthorhombic crystal system with one and four molecules in the asymmetric unit respectively. Both **3a** and **3b** the xanthene rings are similar but they differ in the position of cyano group on the phenyl ring, **3a** contains 3-cyano phenyl ring whereas **3b** contains 4-cyano phenyl ring as substituents. In compound **3a** and **3b** the aryl ring is positioned axially to the xanthene ring with a dihedral angle of 87.83° and 89.91° respectively. Aryl rings in both the compounds are projected away from the plane of the xanthene ring.

compound 3a, the central In pyran ring R (O1/C8/C9/C16/C17/C24) of the xanthene moiety is in boat conformation, with atoms C8 and O2 displaced by 0.124(2)Å and 0.103(0)Å, respectively from the mean plane of the other four atoms (C9/C16/C17/C24) and the two outer rings, ring A (C17/C18/C19/C22/C23/C24), and ring C (C9/C10/C11/C12/C15/C16) are in sofa conformations. The two cyclohexenone rings adopt sofa conformation in ring A, C19 atom lies 0.592(4) Å above the plane from the remaining 5 atoms of the ring A (C17/C18/C22/C23/C24) and in ring C, C12 atom by 0.618(5) Å above the plane of the remaining 5 atoms of the ring (C9/C10/C11/C15/C16).

In compound **3b** the central pyran ring of the xanthene moiety adopts boat conformations with O1 and C9 atoms displaced by 0.085Å and 0.185 Å respectively from the mean plane of the other four atoms C1/C6/C9/C10/C15 and the two cyclohexenone rings adopt sofa conformation. Ring A (C1/C2/C3/C4/C5/C6), shows sofa conformation with C4 atom displaced by 0.645(4)Å from the remaining 5 atoms of the ring (C1/C2/C3/C5/C6) similarly, in ring C (C10/C11/C12/C13/C14/C15) sofa conformation is observed with C13 atom displaced by 0.625(4)Å from the remaining 5 atoms of the ring C10/C11/C12/C14/C15. The crystal structure of **3a** is stabilised by one C-H•••N and one C-H•••O intermolecular interactions (Fig. 3), whereas the crystal structure of **3b** is stabilised only by three C-H•••O intermolecular interactions (Fig. 4).

Compound Codes.	Compounds	Yield (%)	Time(mins)	Obs. mp(°C)	Lit. mp(°C) [Ref]
3a.		85	60	204-206	[-]
3b.		88	55	205-207	[-]
3c.		95	50	204-206	(205-207 [41])
3d.		91	50	232-234	(231–233 [42])
3e.		93	55	172-174	(170-172 [43])
3f.		98	60	224-226	(226-227 [41])
3g.		86	55	225-227	(224-225 [41]) (continued on next page)

 Table 3
 Isolated Yields and time duration for formation of 9-aryl-1H-xanthendiones 3a-3j.

Table 3(continued)







Fig. 1. A plausible mechanism for the formation of xanthenedione with boric acid 3a-j.

Table 4	
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Crystal data and refinement parameters for compounds 3a and 3b.

Compound code	3a	3b
CCDC No.	1918601	1960240
Empirical formula	C ₂₄ H ₂₅ N O ₃	C ₂₄ H ₂₅ N O ₃
Formula weight	375.45	375.45
Temperature K	298(2)	293K
Wavelength Å	0.71076	0.71073 Å
Crystal system	Triclinic	Orthorhombic
space group	P-1	Pbcn
a [Å]	7.546(5)	15.4678(5) A
b [Å]	10.604(9)	10.9796(4) A
c [Å]	13.753(10)	24.2521(8) A
α(°)	87.57	90
β(°)	78.28	90
γ(°)	73.67	90
Volume Å ⁻³	1034.0(1)	4118.7(2)
Z	2	8
Calculated density Mg/m ³	1.206	1.211
F(000)	400	1600
Theta range/ (°) deg.	2.96 to 29.10	3.33 to 26.00
Limiting indices	-9<=h<=10,	-19<=h<=15,
	-14<=k<=14,	-13<=k<=12,
	-18<=l<=18	-25<=l<=29
Reflections collected / unique	20161 / 5497	17535 / 4044
R(int)	0.0653	0.0289
Completeness to theta	99.7 %	99.8
Max. and min. transmission	0.997 and 0.988	% 0.9760 and 0.9744
Data / restraints / parameters	5497 / 0 / 258	4044 / 0 / 257
Goodness-of-fit on F ²	1.018	1.048
Final R indices [I>2sigma(I)]	R1 = 0.0638,	R1 = 0.0446,
R1	wR2 = 0.1285	wR2 = 0.1095
R indices (all data) R1	R1 = 0.1504,	R1 = 0.0766,
	wR2 = 0.1613	wR2 = 0.1211
Largest diff. peak and hole $(e, \text{ Å}^{-3})$	0.190 and -0.207	0.136 and -0.136

Table 5

Non-bonded interactions and possible hydrogen bonds (Å) for compound **3a** (D-donor; A-acceptor; H-hydrogen).

$D-H \bullet \bullet \bullet A$	D—H	H● ● ●A	D• • •A	D−H• • •A
C3-H3 O3 ⁱ	0.930	3.438	2.553	159.16
C22-H22B N1 ⁱ	0.970	3.588	2.720	149.39

Symmetry codes: (i) -x+2,-y+1,-z.

Table 6

Non-bonded interactions and possible hydrogen bonds (Å) for compound **3b.** (D-donor; A-acceptor; H-hydrogen).

D−H• • •A	D—H	H• • •A	D• • •A	$D-H \bullet \bullet A$
C5-H5A…O2 ⁱ	0.970	2.690	3.605	157.48
C20-H20A…O3 ⁱⁱ	0.930	2.388	3.275	159.29
C12-H12B…O2 ⁱⁱⁱ	0.970	2.612	3.565	148.07
Symmetry codes: (i) -x+1/2,	-y-1/2, +z	(ii) -x+1,	-y+1, -z+1 (iii)

x+1/2, -y+1/2, -z+1

5.3. Hirshfeld surface analyses

In order to study the intermolecular interactions in compound **3a** and **3b**, Hirshfeld surface (HS) analysis and related 2D finger plots were calculated using Crystal Explorer 17 [37] by submitting the crystallographic information file (CIF) of compounds **3a** and **3b**. Surface features which are characteristic of different types of intermolecular interactions can be identified and these features can be visualized by colour coding distances from the surface to the nearest atom exterior (d_e plots) or interior (d_i plots) [38-40]. The d_{norm} mapped on the Hirshfeld surfaces were generated with colour scale

in between -0.1426au (blue) to 1.7279au (red) respectively for the compound **3a** and -0.2719au (blue) to 1.4982au (red) respectively for the compound **3b**.

The intermolecular interactions in compound **3a** and **3b** are visualized by mapping the HS with different properties like d_e , d_{norm} , curvedness mapped, fragment patch mapped, and shape index in Fig. 5 and 6 [44]. In HS with the d_{norm} (Fig. 5 and 6) white colour surface indicate the contacts with the distances equal to the sum of the van der Waals radii and the red and blue colour indicate the distances shorter and longer than the van der Waals radii respectively.

All the percentages of the 2D fingerprint plot for compound 3a and 3b are shown in (Fig. 7). Fig. 8 and 9 represents two dimensional fingerprint plots (FP) with de and di distances in the range 0.6-2.4Å displaying different intermolecular interactions. Where d_i is the closest internal distance from a given point on the Hirshfeld surface and de is the closest external contacts. The finger print reveals the contribution of each individual intermolecular contact to the surface which can be identified through colour codes (frequency of presence). If $d_i > d_e$ then this represents the dark regions on the surface are due to interaction of hydrogen bond acceptors. Similarly, the regions with $d_e > d_i$ value are due to the hydrogen bond acceptors. The white colour indicates no occurrence, blue indicates some occurrence, green and red indicates more frequent occurrence of any given (di, de) pair. From the total contributions for both compounds 3a and 3b the H-H contacts has maximum and O-C has minimum contributions. Similarly the C-H, O-H and N-H contacts also contribute to the total area of the surface as shown in Fig. 7 for both compound 3a and 3b. Fig. 10



Fig. 2. ORTEP view of compounds 3a and 3b, showing 50% probability ellipsoids and the atom-numbering scheme.

Fig. 7 clearly indicates that, intermolecular interactions contributed by 0•••0, 0•••C, 0•••H, C•••N, C•••H, C•••C, H•••H and N•••H, the maximum contribution are given by H•••H (54.7%) and 0•••H (18.3%) followed by N...H (13.3%), C•••H (9.8%), C•••C (3.4%), C•••N (0.3%), O•••O (0.1%) and O•••C (0.1%) in compound **3a.** However in compound **3b**, intermolecular interactions are contributed by 0•••0, 0•••C, O•••H, O•••N, C•••N, C•••H, C•••C, H•••H, N•••H, and N•••N, the maximum contribution are given by H•••H (53.7%) and O•••H (17.6%) followed by C•••H (14.5%), N•••H (10.8%),O•••N (1.0%), C•••C (0.7%), O•••O (0.6%), C•••N (0.6%), N•••N (0.4%) and C•••O (0.1%). The inter contact distances obtained from Hirshfeld analysis are in good correlation with the single crystal analysis. The contributions of different atoms are shown in (Fig. 7). The higher amount of H•••H interactions in these compounds show that van der Waals interactions also plays a major role in the crystal packing (Fig. 3 and 4). Interestingly, here we have found that in compound **3a** fingerprint plots of O•••N, and N•••N were not found (Fig. 7). Consequently, the contact analysis for the compound **3a** and **3b** suggests that the C-H•••O hydrogen bonds are the driving force in molecular arrangement and crystal packing formation.

5.4. Molecular geometry optimizations

The structure of the compounds **3a** and **3b** was optimized by DFT calculations using the B3LYP hybrid functional with 6-311+G (d, p) basis set. The comparison of selected optimized geometrical parameters such as bond length, bond angle, and torsion angle, with those parameters obtained from XRD studies, are listed in supplimentary file (Tables 7-12). The minor deviations observed between the theoretically calculated and experimentally determined values can be accounted for the differences in the molecular environment between the crystalline phase and gas phase.

5.5. Frontier molecular orbital analysis

HOMO and LUMO orbitals of compounds **3a** and **3b** are shown in Fig. 11 and 12 respectively.

Molecular orbital energy and frontier molecular orbital energy levels are calculated by 6-311+G (d.p) level. The obtained energy values are in atomic units (a.u.) and those values have been converted into electron volt (eV) by making use of the conversion factors as 1 a.u. = 27.211396132 eV. The calculated HOMO and LUMO energies were found to be -6.1239 eV and -2.1978 eV respectively and energy gap of 3.9261 eV for compound **3a** whereas for the compound **3b** HOMO and LUMO energies are -6.9135 eV and -2.2699 eV respectively and energy gap is 4.6436 eV. This large energy gap value for the compound **3b** is an assertion for its high stability.

The energy difference between the HOMO and LUMO orbitals is called the energy gap (ΔE) which is 3.9261 eV and 4.6436 eV for the compound **3a** and **3b** respectively, which is important in expecting the stability and reactivity of the compound. If the gap is large the compound is expected to have high stability and low reactivity whereas when the gap is small the compound is expected to have less stability and high reactivity [45]. The importance of the FMOs is in determining the electronic properties, optical properties, and chemical reactions. The energy of the highest occupied molecular orbital (HOMO) is related to the ionization potential while the energy of the lowest unoccupied molecular orbital (LUMO) is related to the electronic affinity.

The typically important global reactivity parameters related to frontier molecular orbital energies such as chemical hardness (η), electronegativity (χ), electronic chemical potential (μ), global electrophilicity index (ω) were calculated from HOMO-LUMO energy values from equations [46]. The magnitude of global reactivity descriptor values are tabulated in (Table 13).

5.6. Atomic charge analysis

The Mulliken charge distributions for the compounds have been calculated using 6-311+G (d,p) level shown in (Table 14 and 15). In the compounds **3a** and **3b** the magnitude of the carbon Mulliken charges, was found to be either positive or negative, ranging from -1.257 and 1.572 for the compound **3a** and -1.630 to 2.141 for the compound **3b**. The most positive charge is over carbon (C4=1.572) atom in compound **3a** and (C21= 2.141) atom in compound **3b**. The nitrogen and oxygen atoms have negative charges.



Fig. 3. Packing of the compound 3a showing intermolecular C-H•••N and C-H•••O interactions.



Fig. 4. Packing of the compound 3b showing intermolecular C-H•••O interactions.

5.7. Molecular electrostatic potential analysis

The molecular electrostatic potential (MEP) analysis can be regarded as a powerful tool for identifying the possible interaction sites around a molecule. One of the most interesting features of quantum chemistry is the ability to explain the reactivity of compounds under investigation. It determines the reactivity of a chemical system by predicting electrophilic as well as nucleophilic sites in target molecules. The computed MEP using 6-311+G (d,p) level of DFT is shown in (Fig. 13) The MEP surface allows us to visualize the various regions of a molecule. The charge distribution helps to determine the molecular interaction and the nature of the chemical bond. The positive area of the MEP is a nucleophilic site, while the negative region is associated with an electrophilic site. The (Fig. 13) shows the negative charges are more and they are concentrated around the nitrogen atom. The colour code of the map is in the range between -6.280×10^{-2} a.u. (Deepest red) and -6.280 \times 10⁻² a.u. (Deepest blue) in compound **3a** and -5.901 \times 10⁻² a.u. (Deepest red) and 5.901 \times 10⁻² a.u. (Deepest blue) in compound **3b** in the maps, the most negative region on the MEP surface of the compound $\mathbf{3a}$ and $\mathbf{3b}$ are associated with the lone-pairs of the nitrogen atom.

6. Conclusion

In conclusion, the present method is an operationally simple and clean procedure for the synthesis of xanthenediones using a



Fig. 5. d_{norm} mapped, curvedness mapped, fragment patch mapped and shape index mapped on Hirshfeld surface respectively of the compound 3a.



Fig. 6. d_{norm} mapped, curvedness mapped, fragment patch mapped and shape index mapped on Hirshfeld surface respectively of the compound 3b.



Fig. 7. Percentage of finger prints plots of selected interactions of compound 3a and 3b.



Fig. 8. Finger print plots of selected interactions of compound 3a.

catalytic amount of boric acid. In addition, the low cost, easy availability, low toxicity, moderate Lewis acidity and moisture compatibility of the catalyst, excellent yields of products, water solubility and short reaction time makes this methodology a valid contribution to the existing processes in the field of synthesis of xanthenedione derivatives. Xanthenedione derivatives were further characterized by means of various spectroscopic tools like ESI- MS, ¹H and ¹³C NMR and two representative compounds **3a** and **3b** were confirmed by single crystal X-ray diffraction studies. The molecular structure is stabilized by intermolecular N-H^{...}O and C-H^{...}O hydrogen bonds. The three dimensional d_{norm} and 2D finger-print plots from Hirshfeld were studied extensively to understand the intermolecular interactions. The Hirshfeld surface analysis disclose that H-H interactions have maximum contribution to the in-



(i) O···O- 0.6%; (ii) O···C- 0.1%; (iii) O···H- 17.6%; (iv) O···N- 1.0%; (v) C···N- 0.6%;



(vi) C···H- 14.5%; (vii) C···C- 0.7%; (viii) H...H- 53.7%; (ix) N...H- 10.8%; (x) N...N- 0.4%





Fig. 10. DFT optimized molecular structure of the compound 3a and 3b.

Table 13	
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The energy values of global reactivity descriptors.

Parameter	Compound 3a Value in eV	Compound 3b Value in eV
E _{LUMO}	-2.1978	-2.2699
E _{HOMO}	-6.1239	-6.9135
ΔE	3.9261	4.6436
Chemical Hardness (η)	1.9630	2.3218
Electronegativity(χ)	4.1608	4.5917
Chemical Potential (μ)	-4.1608	-4.5917
Chemical Softness(s)	0.2547	0.2153
Global electrophilicity $index(\omega)$	4.4096	4.5403

termolecular interactions. Further, the molecule was geometrically optimized using B3LYP/ 6-31G (d,p) level of theory. The Mulliken atomic charges and MEP were analysed for the nucleophilic and electrophilic regions of the molecular surface. The HS and MEP analysis indicated the presence of a strong C-H...O hydrogen bond formation. While the 2D fingerprint plot provides percentage con-

tribution of each individual atom-to-atom interactions. Moreover, the HOMO-LUMO energy gap suggests a good stability of these compounds. The correlation between the bond lengths and bond angle parameters obtained from crystallographic studies and from theoretical calculations are in good agreement with the optimized structures. 7. Supplementary data

ccdc.cam.ac.uk).



Fig. 11. HOMO-LUMO orbitals of compound 3a.

Supplementary crystallographic data for this article in CIF format are available at the Electronic Supplementary Publication from Cambridge Crystallographic Data Centre (**CCDC Nos: 3a** 1918601 and **3b** 1960240). This data can be obtained free of charge http: //www.ccdc.cam.ac.uk/conts/retrieving.html, from the Cambridge Crystallographic Data Centre, 12 Union Rood, Cambridge CB2 1EZ, UK (Fax: (international): +44 1223/336 033; email: deposit @ Atomic charge analysis for compound **3a**.

Atom	Mulliken charge	Atom	Mulliken charge
C1	-0.645	C13	-0.504
C2	-0.371	C14	-0.473
C3	-0.348	C15	-0.34
C4	1.572	C16	-0.487
C5	-1.257	C17	-0.362
C6	-0.242	C18	-0.426
C7	1.33	C19	0.475
C8	0.278	C20	-0.447
C9	0.521	C21	-0.509
C10	-0.415	C22	-0.594
C11	-0.636	C23	-0.23
C12	0.306	C24	0.555
01	-0.214	03	-0.233
02	-0.39	N1	-0.197



Fig. 13. MEP surface of the compound 3a and 3b respectively.

Table 15

P	Atomic charge analysis for compound 3b .				
	Atom	Mulliken charge	Atom	Mulliken charge	
	C1	0.885	C10	0.885	
	C2	-0.573	C11	-0.573	
	C3	-0.512	C12	-0.513	
	C4	0.356	C13	0.356	
	C5	-0.45	C14	-0.45	
	C6	-0.55	C15	-0.55	
	C7	-0.506	C16	-0.506	
	C8	-0.501	C17	-0.501	
	C9	0.261	C23	-0.087	
	02	-0.209	03	-0.209	
	C18	1.177	C21	2.141	
	C19	0.136	C22	-1.006	
	C20	-0.588	C24	-1.63	
	01	-0.033	N1	-0.189	

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Declaration of competing interest

The author 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

R Shashi: Conceptualization, Methodology, Writing - original draft, Investigation, Software. Noor Shahina Begum: Supervision, Visualization, Validation. Anoop Kumar Panday: Formal analysis.

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