

# Synthesis, Characterization and Computational Study of Dimethoxychalcone

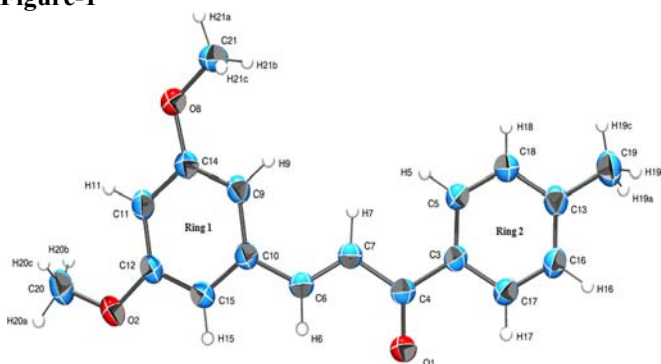
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**Abstract**—Chalcones are an important class of medicinal compounds and are known for taking part in various biological activities as in anti-inflammatory, anti-leishmania, antimitotic, and antiviral. Chemically, chalcones consist of open-chain flavonoids in which the two aromatic rings are joined by a three-carbon  $\alpha$ ,  $\beta$ -unsaturated carbonyl system. The wide action spectrum has attracted our attention to synthesize, crystallize, and characterize the dimethoxy-chalcone  $C_{18}H_{18}O_3$ . The synthesised chalcone crystallizes in the centrosymmetric space group  $P21/c$ . The molecule is a chalcone with 3, 5-dimethoxyphenyl and 4-methylphenyl rings bonded at the opposite ends of a  $-\text{CO}-\text{CH}=\text{CH}-$  group. The ellipsoid displacement plot with the numbering scheme is presented in graphical abstract below (Figure-1). Aiming to understand the process of crystal lattice stabilization, a combination of technique has been used including X-ray diffraction, infrared spectroscopy and computational molecular modeling. The theoretical calculations were carried out by the density functional method (DFT) with the M06-2X functional, with the 6-311+G(d, p) basis set. The vibrational wavenumbers were calculated and the scaled values were compared with experimental FT-IR spectrum. The intermolecular interactions were quantified and intercontacts in the crystal structure were analyzed using Hirshfeld surfaces. Bond distances and angles described by the X-ray diffraction and theoretical calculation are very similar. X-ray geometry parameters (bond lengths, bond angles, and torsion angles) were compared with fully optimized geometric parameters, and the results are very similar. The C-H...O contacts contributing to assemble the supramolecular architecture are also responsible for the molecular structure assembly.

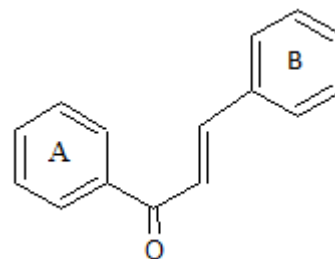
**Keywords:** DFT, Dimethoxy-chalcone, Infrared spectroscopy, X-ray diffraction

**Figure-1**



## 1. INTRODUCTION

Chalcones are pharmacologically valuable moieties possessing 1, 3-diphenyl prop-2-ene-1-one ( $-\text{CH}=\text{CH}-\text{CO}-$ ) as a core structure in which two aromatic rings are linked by first and third carbon of  $\alpha$ ,  $\beta$  unsaturated carbonyl skeleton.



(General structure of chalcones (1, 3-diphenyl prop-2-ene-1-one))

Recently many chalcones have been reported to have antimicrobial activity due to the presence of a reactive  $\alpha$ ,  $\beta$  unsaturated keto skeleton [1]. In recent years a variety of chalcones have been reviewed for their cytotoxic, anticancer chemopreventive and mutagenic as well as antiviral, anti-insecticidal and enzyme inhibitory properties [2, 3]. A number of chalcones having hydroxyl, alkoxy groups in different position have been reported to possess antibacterial [4], anti-ulcer [5], antifungal [6], antioxidant [7], vasodilatory [8], antimitotic [9], antimalarial [10], anti-leishmanial [11]. Appreciation of these findings motivated us to synthesize chalcones derivatives suitable for biological application. Present paper deals with synthesis, structural characterization, and M06-2X/6-311+G(d, p) calculations of (E)-3-(3, 5-dimethoxyphenyl)-1-(4-methylphenyl)prop-2-ene-1-one ( $C_{18}H_{18}O_3$ ). In order to understand the nature of crystal packing and to describe the molecular sites where electrophilic and nucleophilic reactions can take place and the hydrogen-bonding interactions, the molecular electrostatic potential mapping was performed on title compound at the same level of theory. The M06-2X/6-311+G(d, p) calculations of the vibrational modes were carried out in order to support the

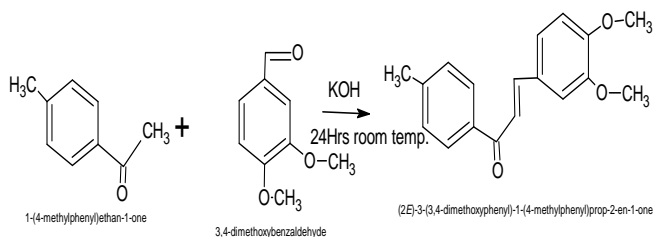
spectrum assignment of the (E)-3-(3, 5-dimethoxyphenyl) 1-(4-methylphenyl) prop-2-en-1-one. Finally, the computations of the geometric and electronic properties presented here are very important to shed light on the understanding of the structure-activity relationship [10] for this new compound.

## 2. EXPERIMENTAL AND COMPUTATIONAL METHODS

### 2.1 General Procedure for the Preparation of Chalcones:

Equimolar quantities (0.01mol) of 4-methylacetophenone and respective 3, 4-dimethoxybenzaldehyde were mixed and dissolved in minimum amount (3 ml) of alcohol. To this, aqueous potassium hydroxide solution (0.03 mole) was added slowly and mixed occasionally for 24 h, at room temperature. After that the reaction mixture was poured into crushed ice and neutralized with dil. HCl (10%). The precipitate was washed with EtOH and purified by recrystallization and chromatographic technique [8]. Reaction pathway is represented in scheme-1

#### SCHEME-1



The synthesised chalcone is obtained as yellow solid

MP<sub>s</sub>: 85.2–87.6 °C

**<sup>1</sup>H-NMR** (500MHz)(CDCl<sub>3</sub>):δ (ppm) 2, 46(s, 3 H, CH<sub>3</sub>Ph)3, 86(s, 6 H, OCH<sub>3</sub>Ph) 6, 55 (t, 1H, PhCH, J=2, 4 Hz) 6, 80 (d, 2H, PhCH, J=2, 4 Hz) 7.33 (d, 2 H, PhOCH<sub>3</sub>J=8.4 Hz) 7.50 (d, 1H, CHCO, J=15.6Hz) 7.73(d, 1H, CHPh, J=15.6Hz) 7.95 (d, 2H, PhOCH<sub>3</sub>, J=8.4 Hz)

**IR (KBr)** cm<sup>-1</sup>: 2940; 1657 (C=O); 1593; 1426.

**Table 1** Crystal data and structure refinement for C<sub>18</sub>H<sub>18</sub>O<sub>3</sub>

Formula weight	282.32 u.a.
Temperature	293 K
Wavelength	0.71073 Å
Crystal system	Monoclinic Space group P21/c
Unit cell dimensions	a =16.8489(4) Å
	b =11.5390(3) Å
	c =8.0891(2) Å
	β=103.506(2)0

Volume	1529.18 Å <sup>3</sup>
Z, calculated density	4, 1.29 mg/m <sup>3</sup>
Absorption coefficient	0.083 mm <sup>-1</sup> F (000) 600.0
Reflections collected/unique	30, 952/3127
Refinement method	direct methods
Goodness-of-fit	on F2 1.020
Final R indices	[I > 2σ (I)] 0.048
R indices	(all data) 0

## 3. RESULTS AND DISCUSSIONS

### 3.1 MOLECULAR STRUCTURE

The dimethoxy-chalcone C<sub>18</sub>H<sub>18</sub>O<sub>3</sub> crystallizes in the centrosymmetric spacegroup P21/c. The molecule is a chalcone with 3, 5-dimethoxyphenyl and 4-methylphenyl rings bonded at the opposite ends of a –CO–CH=CH– group. The ellipsoid displacement plot with the numbering scheme is presented in Fig. 1. X-ray geometry parameters (bond lengths, bond angles, and torsion angles) were compared with fully optimized geometric parameters, and the results are very similar. The optimized and experimental geometry are presented in Table 2.

**Table 2:** The calculated and experimental geometric parameters for C<sub>18</sub>H<sub>18</sub>O<sub>3</sub>

Bond distances (°Å)	X-ray	DFT	Bond angles (°)	X-ray	DFT
	C3-C17	1.397(2)		1.398	C4-C3-C5
C3-C4	1.486(2)	1.498	C4-C3-C17	118.9(1)	118.2
C4-O1	1.228(2)	1.214	C5-C3-C17	117.6(1)	118.9
C4-C7	1.477(3)	1.488	O1-C4-C3	120.1(1)	120.3
C5-C18	1.377(2)	1.391	O1-C4-C7	1204.4(1)	121.5
C6-C7	1.327(3)	1.338	C3-C4-C7	119.4(1)	118.1
C6-C10	1.465(2)	1.468	C3-C5-C18	121.2(1)	120.4
C9-C14	1.377(2)	1.384	C7-C6-C10	127.2(1)	126.8
C9-C10	1.406(2)	1.408	C4-C7-C6	121.5(1)	120.1
C10-C15	1.393(2)	1.386	C14-C8-C21	117.9(1)	117.8
C11-C12	1.377(3)	1.384	C10-C9-C14	118.7(1)	119.1
C11-C14	1.394(2)	1.403	C6-C10-C15	118.1(1)	118.1
C12-O2	1.365(2)	1.355	C9-C10-C15	120.1(1)	120.1
C12-C15	1.393(2)	1.401	C12-C11-C14	119.5(1)	119.2
C13-C18	1.387(3)	1.393	O2-C12-C11	124.5(1)	124.1
C13-C16	1.387(2)	1.399	O2-C12-C15	115.3(1)	115.6
C13-C19	1.505(2)	1.506	C11-C12-C15	120.2(1)	120.2
C14-O8	1.366(2)	1.357	C16-C13-C18	117.5(1)	118.4
C16-C17	1.372(2)	1.384	C16-C13-C19	121.6(2)	120.3
C20-O2	1.425(3)	1.413	C18-C13-C19	120.9(2)	121.3

C-21-O8	1.425(2)	1.412	O8-C14-C9	124.3(1)	124.3
			O8-C14-C11	114.4(1)	114.5
			C9-C14-C11	121.3(1)	121.1
			C10-C15-C12	120.1(1)	120.1
			C13-C16-C17	121.8(1)	120.9
			C3-C17-C16	120.7(2)	120.4
			C5-C18-C13	121.2(1)	120.9

The potential intermolecular interactions of the synthesised chalcone is visualized using Hirshfeld surface analysis. This approach is a graphical tool for visualization and understanding of intermolecular interactions. The intermolecular contacts are estimated using WingX. The Hirshfeld surface analysis, with finger plots and electrostatic potential map, reveals the intermolecular contacts and distribution of electrostatic potential of the synthesised chalcone. This helps to understand the molecules packing and the crystal stabilization.

### 3.2 Infrared spectrum

The vibrational frequencies (theoretical and experimental) in the infrared range, are in good agreement, from which it was possible to characterize the main absorbent groups. The observed discrepancies are due to the fact that calculations were made for a free molecule in a vacuum, while experiments were carried out in a solid sample. It is well known fact that the DFT calculations over estimate the vibrational frequencies systematically [17], and the use of a proper scaling factor for M06-2X, equal to 0.947 [18] provides more reliable values to compare to the experimental data. The heteroaromatic structure shows the presence of CH stretching vibrations in the 3000–3175 cm<sup>-1</sup> range, which is the characteristic region for the identification of CH stretching vibrations [19]. In this region, the bands are not affected appreciably by the nature of the substituents. The ring CC stretching vibrations occur in the region 1321–1686 cm<sup>-1</sup> [19-20]. The CC stretching modes for the A and B rings are observed at 1527 and 1686 cm<sup>-1</sup>. The ring stretching vibrations, which are highly characteristic of the aromatic ring itself, are very important in the spectrum of benzene and its derivatives. The prominent band between 1625 and 1650 cm<sup>-1</sup> is characteristic of the  $\alpha$ ,  $\beta$ -unsaturated carbonyl group of a chalcone. In the present work, the calculated values are 1701 cm<sup>-1</sup> for unscaled and 1611 cm<sup>-1</sup> for scaled frequency. The band in 1792 cm<sup>-1</sup> is characteristic of the C=O stretching mode [19].

### 3.3 Frontier molecular orbitals

The highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) energies are directly related to the ability to donate and accept electrons. The LUMO energy is directly related with the molecular electron affinity and characterizes the susceptibility of the molecule toward an attack by a nucleophile. Both the HOMO and the LUMO energies are important in radical reactions [12]. The energy difference between HOMO and LUMO is an

important chemical stability index [13]. A large HOMO-LUMO gap implies high stability with respect to chemical reaction [14]. They are also used to describe chemical softness and hardness. The plot of the frontier molecular orbital helps us to have a better understanding of the nature of the chemical bond scheme [15]. For the synthesised chalcone, the HOMO (-8.7828 eV) orbital is localized entirely on the R1 ring (dimethoxyphenyl group), while the LUMO (-6.4783 eV) orbital is spread out throughout the molecule, except for the H<sub>3</sub>CO and CH<sub>3</sub> groups. These orbitals are  $\pi$ -bonding and  $\pi$ -antibonding character, respectively. The high gap energy (2.3045 eV) indicate that this compound has high chemical stability and high excitation energies.

The hardness ( $\eta$ ) of a molecule is given by [12]:

$$\eta^4 = \frac{E_{LUMO} - E_{HOMO}}{2}$$

where  $E_{LUMO}$  and  $E_{HOMO}$  are the energies of the LUMO and HOMO orbitals, respectively. The chemical hardness is directly correlated to the chemical stability. The molecules having a small or large energy gap are known as soft or hard molecules, respectively. The hard molecules are not more polarizable than the soft ones because they need a big energy to excitation [16]. The value of the energy gap between the HOMO and LUMO is 2.3045 eV and the value of hardness is 1.1522 eV. Compared to the (E)-4-methoxy-2[(p-tolylimino)methyl]phenol molecule [16], which is a Schiff based compound (1.842 eV), the studied molecule presents a smaller hardness.

## 4. CONCLUSIONS

The compound C<sub>18</sub>H<sub>18</sub>O<sub>3</sub> was crystallized in the centrosymmetric space group P21/c, and the DFT analysis of optimized structural parameters showed good agreement to those observed in X-ray diffraction. The molecules are connected by C-H...O hydrogen bonds and the short contacts of the type  $\pi$ ... $\pi$  and C—O... $\pi$  help the crystal packing stabilization. The Hirsh field surface analysis with finger plots and electrostatic potential map reveals the percentage of intermolecular contacts and distribution of electrostatic potential. The diagram helps to understand the reactive behaviour of the compounds. The vibrational FT-IR spectrum of molecule was recorded and assigned with the aid of the experimental and computed vibrational wavenumbers. The comparison of the predicted bands with the experimental results shows an acceptable general agreement. The frontier molecular orbital's and potential electrostatic surface calculated are parameters that provide evidence of the lock and key mechanism on any chemical or biological process that could be of interest. Also, they showed how aromatic rings are regions more likely to interact with nearest neighbour molecule. In summary, a structural characterization of title compound was given in the present paper showing that the M06-2X hybrid density functional are able to supply a variety of very reliable molecular properties.

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