Synthesis of a Novel5, 7-Dichloroto-2-(3, 4-Dimethoxyphenyl)-8-Hydroxy-4*h*-Chromen-4-One, its Characterization and DFT Study

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Abstract: ***Flavonoid Compound is one of the most important biologically active heterocyclic compounds. In view of this, a flavone; 6, 8-dichloro-2-(3, 4-dimethoxyphenyl)-4H-chromen-4-one (DDP) has been synthesized, characterized by 1H NMR, FT-IR and mass spectral analysis. It is studied by using density functional theory (DFT) at B3LYP/6311++G (d, p) basis set. The geometry of the DDP molecule has been optimized by using B3LYP/6-311++G (d, p) basis set and structural parameters on bond lengths and bond angles has been discussed. The FT-IR, ^{1}HNMR and mass spectra of the title compound has been carried out by experiment. Highest Occupied Molecular Orbital and Lowest Unoccupied Molecular Orbital analysis and various quantum chemical parameters are calculated and discussed for the better understanding of behavior of the this molecule.***

Keywords: Flavone, 1HNMR, FT-IR, (DFT) at B3LYP/6311++G(d,p) basis set and Chromen

1. Introduction

Chalcones are synthesized by different methods among these are, Claisen-Schmidt condensation [1], Suzuki coupling reaction [2], Friedal Crafts acylation using α, β unsaturated acid chloride in the presence of Lewis acid [3-5], Claisen-Schmidt condensation under ultra sound irradiation [6]. Naturally occurring α, β unsaturated compounds are synthesized in a single step by Heck reaction in which alkenes react with aryl halides in presence of metal complexes [7]. Dalvi et al. [8] have reported the synthesis of 1-(2-hydroxy-phenyl)-3-piperidine-1-yl-propenones by ultrasonic irradiation. The Claisen-Schmidt condensation is the basic reaction for the synthesis of α, β unsaturated compounds in which boronic acid containing aromatic ketones condense with aromatic aldehyde in presence of soluble alkaline hydroxide [9]. Chromones are synthesized by oxidative cyclisation of α, β unsaturated compounds. The reagents are SeO$_2$ in amyl alcohol, sodium hypobromite, and catalytic iodine in DMSO and washed it with copper chloride.

Doshi et al. carried out [10] synthesis of chromones derivative by oxidative cyclisation of α, β unsaturated compounds using DMSO/I$_2$. α, β unsaturated compounds are oxidatively cyclized [11, 12] to flavanols by Algar-Flynn-Oyamada reaction. Ballesteros and co-workers reported [13] synthesis of chromones derivatives by oxidative cyclisation of α, β unsaturated compounds using SeO$_2$ in DMSO. Auwers synthesized [14] a series of organic reactions forming flavanol from a coumarone.2-acetoxyacetophenones in presence of base forms 1, 3-diketone which upon cyclisation results into flavones [15, 16]. Reactions of o-hydroxyaryl ketones with aromatic anhydrides form flavones or isoflavones [17-18].

The chemistry of α, β unsaturated compounds has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of α, β unsaturated compounds. The name "Chalcones"was given by Kostanecki and Tambor [19]. These compounds are also known as benzalacetophenone or benzylidene acetophenone. In α, β unsaturated compounds, two aromatic rings are joined by an aliphatic three carbon chain. α, β unsaturated compounds bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed α, β unsaturated compounds are unsaturated ketone containing the reactive keto-ethylenic group –CO-CH=CH-. These are coloured compounds because of the presence of the chromophore-CO-CH=CH-, which depends in the presence of other auxochromes. Keeping in mind all these pharmalogical activity, synthetic utility as a synthon, we have synthesized the (2*E*)-1-(3, 5-dichloro-2-hydroxyphenyl)-3-(3, 4-dimethoxyphenyl) prop-2-en-1-one and from this we have synthesized the DDP.

2. Reaction Scheme

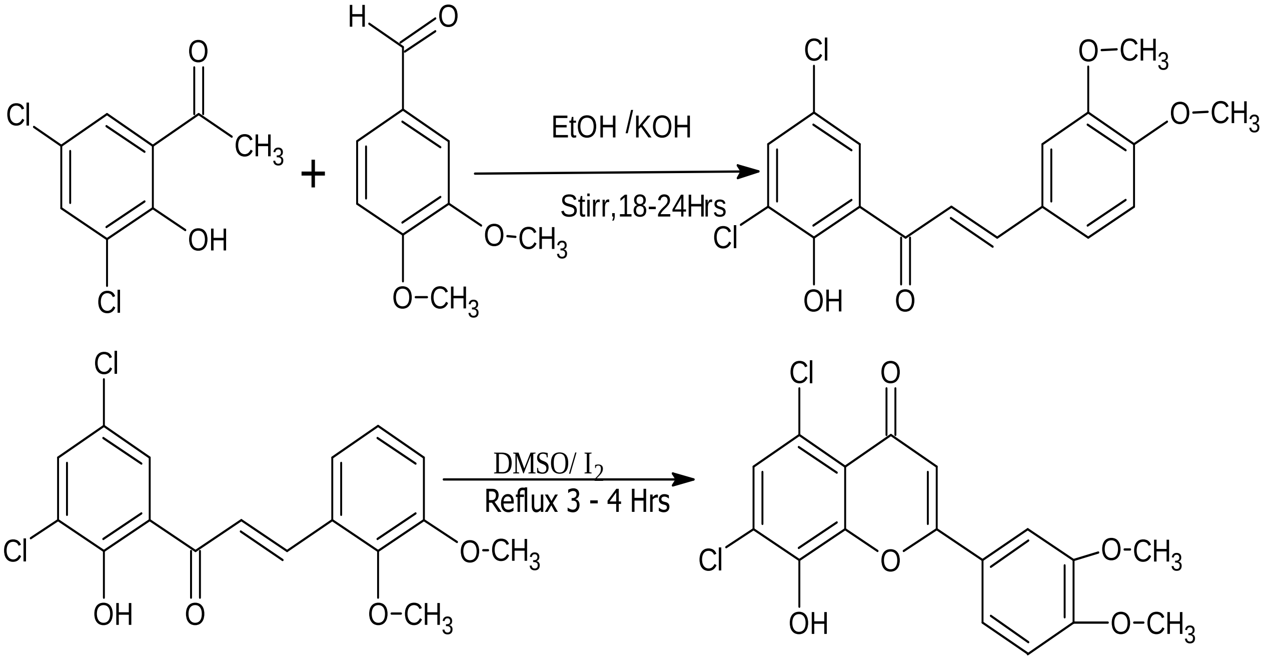


Figure 1: Synthesis of Chromene

3. Preparation of chalcones

Aqueous Potassium Hydroxide (0.02mol) was added to the suspension 1-(3, 5-dichloro-2-hydroxyphenyl) ethanone (0.01mol) and 3, 4-dimetoxy benzaldehyde (0.01mol) in ethyl alcohol. The reaction mixture was stirred at room temperature for overnight. After completion of the reaction (checked) by Thin Layer Chromatography, The reaction mixture was poured onto ice cold water and acidified with HCL (1M). The Solid obtained was filtered (α, β unsaturated ketone) and crystallized from ethyl alcohol to give the product.

3.1 Preparation of Chromen

The compound (0.35g 0.001m) was dissolved in DMSO (20 ml), and a crystal of iodine was added to it. The mixture was refluxed for 40-50 minutes. The solid obtained after dilution with excess of water was filtered, washed with aqueous 20% sodium thiosulphate solution till the product become colorless. Further the product was purified by column chromatography using hexane: ethylacetate (80-20v//v) as an eluent.

3.2 Experimental

Meiting point was incrrected. Infra Red spectrum was recorded on a Perkin Elmer model spectrometer on KBr pellets. Ultra Violet was recorded on Perkin Labindia/UV 3000+ / Visible Spectrometer with methanol as a solvent.1H NMR spectrum was recorded on Nuclear Magnetic Resonance Spectrometer (300 MHZ) varian mercury 300 using CDCCl$_3$ as a solvent and TMS as a internal standard. GC-MS is recorded on Agilent Ion trap. Elemental analysis was carried out on a CHNS (O) Analyzer model (Flash EA 1112) Series. All chemical needed for the synthesis were obtained from commercial source and obtained without further purification of the titled compound.

3.3 Spectroscopic data: 6, 8-dichloro-2-(3, 4-dimethoxyphenyl)-4*H*-chromen-4-one.

Spectral Analysis:
IR (KBr): 3063, (Ar-CH), 1663 (C=O), 1597, 1585, 1518 (C=C), 1217, 1140 (C-O), 783, 847 (C-Cl).
^{1}H NMR: δ 3.97 (S, 3H, OCH$_3$), 3.98 (S, 3H, OCH$_3$), 6.79 (S, 1H, 3-H), 8.09 (d, 1H, 5-H), 7.73 (d, 1H, 7-H), 7.47 (d, 1H, 2`-H), 7.62 (dd, 1 H, 6`-H), 7.01 (d, 1H, 5`-H). **GC-MS (EI):** FW (351.18), M+ (351), M+1 (352).
UV λmax (MeOH), nm (absorbance): 342 (0.373).
GC-MS (EI): FW (351.18), M+ (351), M+1 (352).

3.4 Computational details

DFT study gives us visualization program, the vibrational frequency assignments, bond lengths, bond angles and other parameters were made. All the calculations were done for the optimized structures in gas The DFT calculations were performed on an Intel (R) Pentium (R) Dual Core personal computer using the Gaussian-03W program package [20] without any constraint on the geometry. Geometries of the 2-(4-chlorophenyl)-4*H*-chromen-4-one was first optimized at 6-311++G (d, p) basis set. Optimized structural parameters were used in the geometry optimization at DFT levels with B3LYP (Becke-Lee-Yang-Parr three parameters) to confirm the structure as minima. Using Gauss View 4.1.2 molecular phase.

4. Results and Discussion

The detailed spectral results are tabulated in Table 1.0., 1.1., 1.2. The ^{1}HNMR spectrum, Elemental analysis, FT-IR and GC-MS is carried out in IIT, Powai, Mumbai. The H^1 NMR spectrum predicts types and total number of hydrogen atoms in the molecule. There are total of eleven protons in the title molecule has given the signals as stated in Table 1.2. The elemental analysis of the compound i. e. carbon and hydrogen shows good correlation with theoretical value.

Experimentally formula weight of the compound is observed at (351.18), M+ (351) and M+1 is (352). The ^1H NMR has taken in $CDCl_3$ shows three singlet, two doublet and multiplate for four hydrogen. The infra red spectroscopy determines aromatic hydrogen at 3063 cm^{-1}, carbonyl group at 1663 cm^{-1}, C=C occur at 1597 cm^{-1}, 1585 $cm^{-1}$and at1518 cm^{-1}. C-O occurs at 1217 $cm^{-1}$and 1140 cm^{-1}.783 cm^{-1} and 847 cm^{-1} C-Cl occurs. Theoretically maximum wavelength in methanol as a solvent is observed at 342 with absorbance 0.373.

Table 1: Physical data of title compound

R_1	R_2	R_3	R_4	R_5	R_6	Yield %	M. P. (^{0}C)
Cl	H	Cl	H	OCH_3	OCH_3	66	220-222

Table 1.1: Elemental analysis of the compound

Calculated		Observed	
C %	H %	C %	H %
70.19	3.53	70.09	3.64

Table 1.2: Experimental ^1H NMR chemical shifts (δ) in ppm recorded in $CDCl_3$

Exptl.
2.48 (S, 3H, CH_3), 6.95 (S, 1H, H8), 8.02 (S, 1H, H11),
7.89 (d, 1H, H12), 7.87 (d, 1H, H5),
7.47 – 7.57 (m, 4H, H17, H19, H21 & H22).

Table 1.3: HOMO, LUMO (a. u.), dipole moment (D), η (eV), μ (eV), ω (eV) and SCF energy (a. u.) values of Titled compound by DFT/ B3LYP/6-311++G (d, p) level.

HOMO	LUMO	Energy Gap	Dipole moment (D)	E (RB+HF-LYP), (a. u.)	η (eV)	μ (eV)	ω (eV)
-0.23891	0.-01749	0.22142	4.2380	-2107.1117	0.101965	-0.1282	0.20393

4.1 Global Reactivity parameters

The chemical reactivity descriptors calculated using DFT are Total energy (E), Chemical hardness (n), electronic chemical potential (u) and electrophilicity (ω). These are used to understand the relationship between structure stability, and the global chemical reactivity. The chemical hardness is associated with the stability and reactivity of a chemical system. In a molecule it measures the resistance to change in the electron distribution or charge transfer. On the basis of frontier Molecular Orbital, Chemical hardness corresponds to the gap between the highest molecular orbital (HOMO) and Lowest Unoccupied Molecular

Orbital (LUMO). Chemical hardness is given by approximately using equation.

$$\eta = (\varepsilon\ LUMO-\varepsilon\ HOMO) / 2\text{-------- (1)}$$

Where ε LUMO and ε HOMO are the LUMO and HOMO energies. The larger the HOMO-LUMO energy gap. The harder and more stable / less reactive the molecule. **Table** 1.3 contains the computed Global Reactivity parameters:

$$\mu = (\varepsilon\ LUMO + \varepsilon\ HOMO) / 2\text{-------- (2)}$$

The electronic chemical potential is defined the negative of electronegativity of a molecule and determined using equation 2.

Physically μ describes the escaping tendency of electron from an equilibrium system. Global electrophilicity index (ω) introduced by Parr [21]. **Table** 1.3 gives Global chemical reactivity indices for titled compound is calculated using the electronic chemical potential and chemical hardness as shown in equation 3.

$$\omega = \mu 2/2\eta\text{-------------------- -(3)}$$

Electroplicity index measure the propensity or capability of a species to accept electrons (22, 23]. It is a measure of the stabilizations in energy after a system accepts additional amount of electronic charge from the environment (24).

The frontier molecular orbital of the titled compound shows that compounds are mainly composed of P atomic orbital, so electronic transition corresponds to above electronic spectra are due to n π^* and π π^* electronic transition.

4.2 Bond length and Bond angel

The synthesized compound was subjected geometry optimization in the ground state. The optimized structural parameters such as bond length and bond angles of this compound calculated by DFT/B3LYP 6-311++G9d, p) basis set are listed in **Table** 1.4 in accordance with the atom numbering scheme given in Figure 2.

Table 1.4: lengths (Å) and Bond angles (^{0}) of **title compound** at B3LYP/6-311++G (d, p) level.

Bond length	(Å)	Bond length	(Å)
C1-C2	1.3583	C19-C17	1.4161
C2-C3	1.3976	C14-C17	1.3900
C2-C5	1.4032	C22-O23	1.2260
C5-C9	1.3846	C19-O24	1.3639
C9-C8	1.3992	C17-O31	1.3621
C8-C6	13811	C4-H7	1.0803
C6-C3	1.3997	C6-H10	1.0821

C3-C22	1.4866	C9-H11	1.0813
C22-C4	1.4506	C13-H16	1.0810
C1-C12	1.4698	C15-H20	1.0833
C2-O21	1.3599	C14-H18	1.0800
C1-O21	1.3649	C25-O24	1.4363
C12-C13	1.3982	C25-H26	1.0950
C12-C14	1.4069	C25-H27	1.0890
C13-C15	1.3912	C25-H28	1.0901
C15-C19	1.3900		
Bond angle (^{0})			
C1-O21-C2	120.4120	C1-C12-C13	120.6090
C3-C22-C4	114.0460	C1-C12-C14	120.3220
C2-C5-C9	120.0410	C12-C14-H17	119.5640
C3-C6-C8	119.2950	C12-C13-Cl27	120.0880
C2-C5-Cl25	120.1140	C12-C14-C16	121.0420
C9-C8-CL24	118.6110	C13-C15-C18	121.4130
C5-C2-O21	117.7070	C12-C14-H17	60.2720
C4-C22-O23	123.7500	C15-C18-C16	59.8470
C1-C4-H7	120.2610	C12-C13-C15	117.7020
C3-C6-H10	118.4740	C14-C16-C18	119.0500

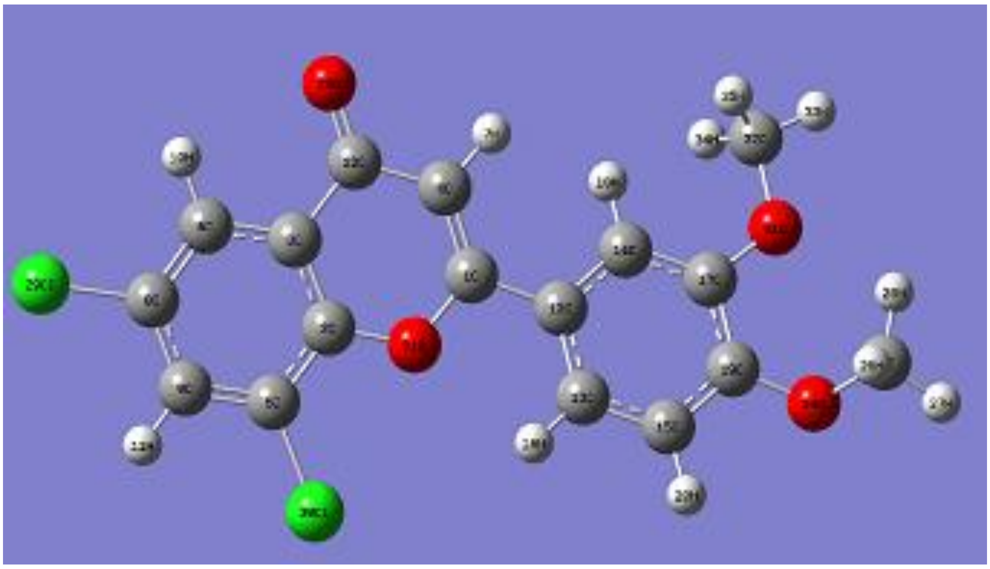


Figure 2: Optimized geometry of Titled compound at 6-311++ (dp) basisi set

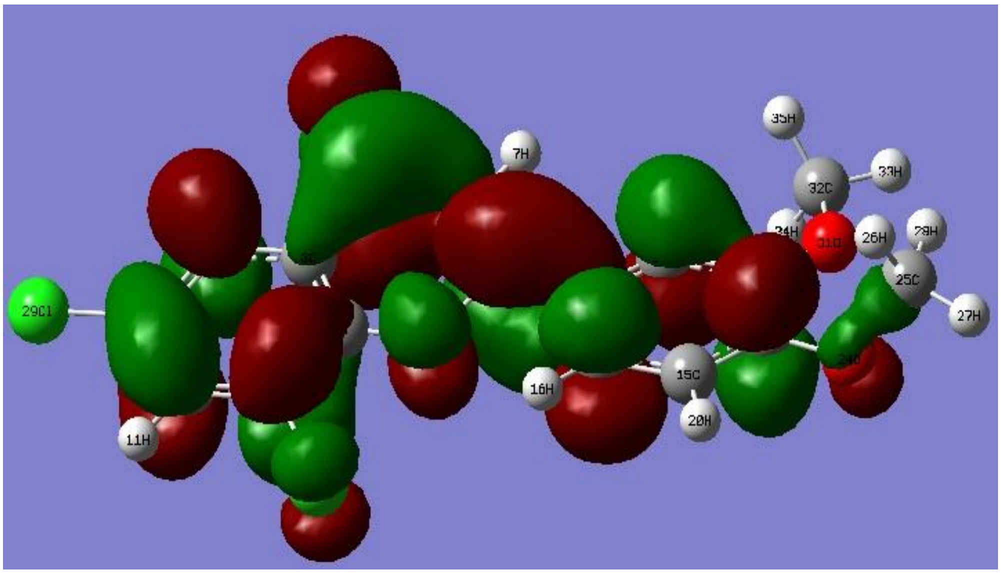


Figure 3: HOMO of Titled Compound at 6-311++ (d, p) basis set

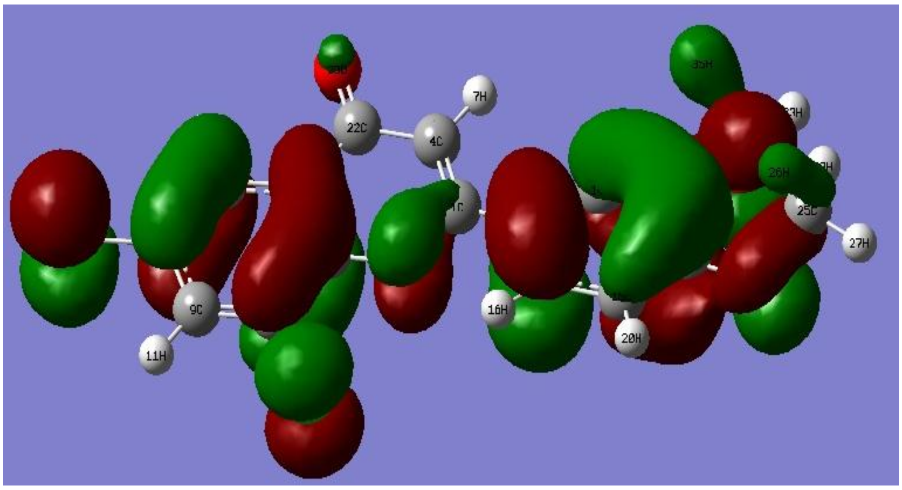
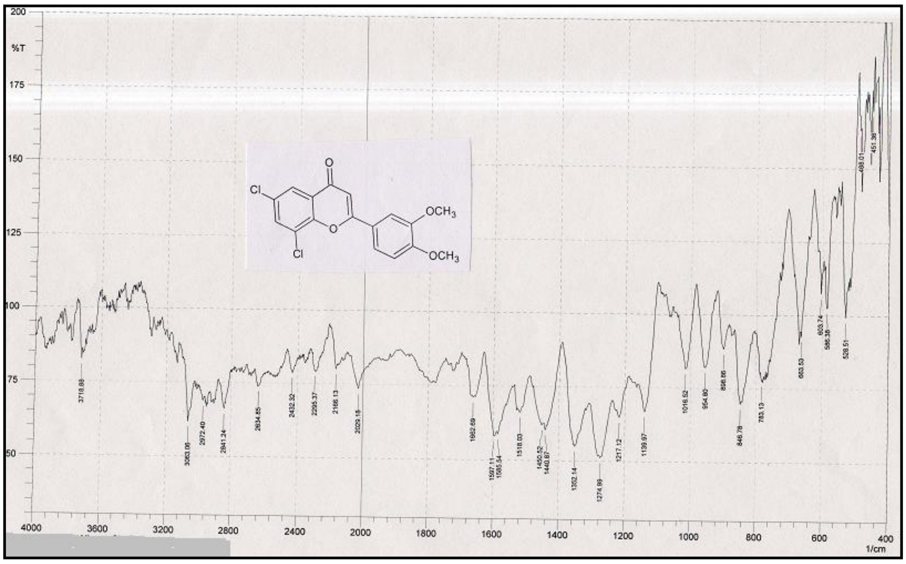


Figure 4: LUMO of Titled Compound at 6-311++ (d, p) basis set



FT-IR

Figure 5: Infra Red spectrum the title compound

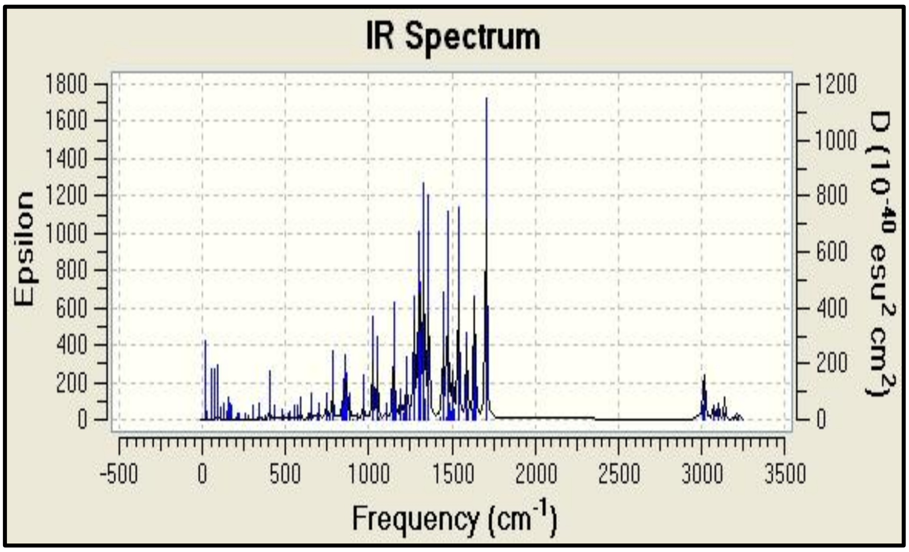


Figure 6: The Theoretical IR spectrum of the title compound

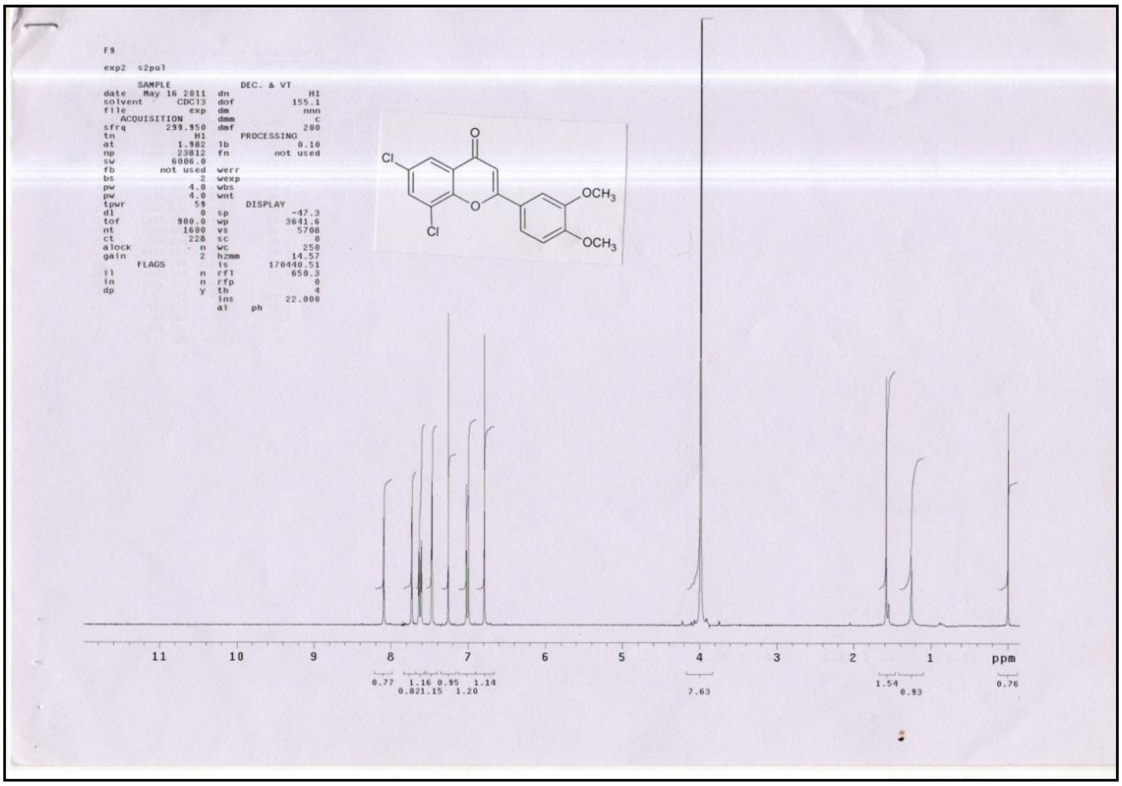


Figure 7: 1H NMR of the title compound: Experimental

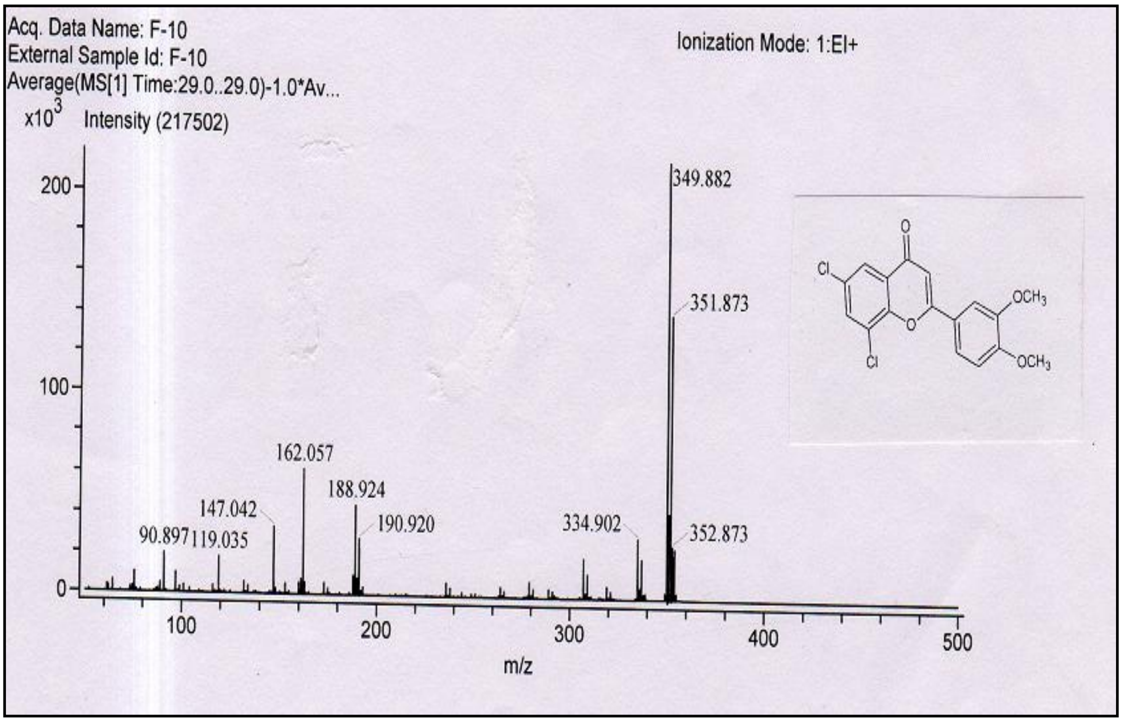


Figure 8: C13 of the titled compound: Experimental

4.3 Mass Fragmentation pattern:

The mass fragmentation pattern of the title compound will show the fragmentation pattern as follows. The molecular formula of the title compound is $C_{17}H_{12}Cl_2O_{4.}$ and having formula weight 351.18. This molecule shows the molecular ion peak at M/Z 351.87and undergoes cleavage to fragments M/Z values at 349.88, 334.90, 190.92, 188.92 and 162.05.

5. Conclusion

The DDP molecule is synthesized from chalcone. The structure of the corresponding molecule is confirmed on the basis of experimental results of ^{1}H NMR, FT-IR and GC-MS spectroscopic analysis. The geometry of the molecule was optimized by using a 6-311G (++) d, p basis set and the geometrical parameters like bond lengths and bond angles have been computed at the same level of theory. The dipole moment of the molecule is-4.2380-The frontier molecular orbital study is discussed and various chemical, electronic and quantum chemical parameters are studied to analyze the chemical reactivity of the DDP molecule. The HOMO-LUMO (0.22142EV) energy gap suggests that the charge transfer phenomenon is taking place within the molecule. Two carbonyl group of the chalcone molecule showing high reactivity towards the nucleophilic reactions.

6. Acknowledgement

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