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Synthesis, Spectroscopic Characterization, Quantum Chemical Study and Antimicrobial Study of (2E) -3-(2, 6-dichlorophenyl) -1-(4-Fluoro) -prop-2-en-1-one

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Abstract

In the present work (2E) -3-(2, 6-dichlorophenyl) -1-(4-Fluoro) -prop-2-en-1-one was Prepared by Claisen-Schmidt condensation .Synthesized molecules were characterized by using FTIR, 1H NMR spectroscopy. Molecular geometry, Vibrational frequency of title compound were calculated using the DFT/B3LYP method with 6-311++G (d, p) basis set. The experimentally obtained FTIR spectra were in good agreement with calculated infrared spectrum. The FMO and molecular electrostatic potential were performed to study the reactivity of molecules at the same level of theory. The synthesized compound shows moderate antimicrobial activity.

Article History

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Keywords:

DFT, Gaussian-03, Chalcone, FMO, UV-Visible.

Introduction

The Chalcone is a simple scaffold found in many naturally occurring compounds mainly in flavonoids and isoflavonoids in plants or can be synthesized in laboratory by different methods. Basically chalcones are alpha, beta unsaturated ketone, in which two aromatic rings joined at 1 and 3 position (1,3-diphenyl-2E-propene-2-one).The two rings of chalcones are interconnected by electrophilic nature of alpha beta unsaturated carbonyl system, which are having complete delocalisation on both aromatic rings. It exists as cis and trans isomer in which trans isomer is thermodynamically more stable. They display a wide range of pharmacological

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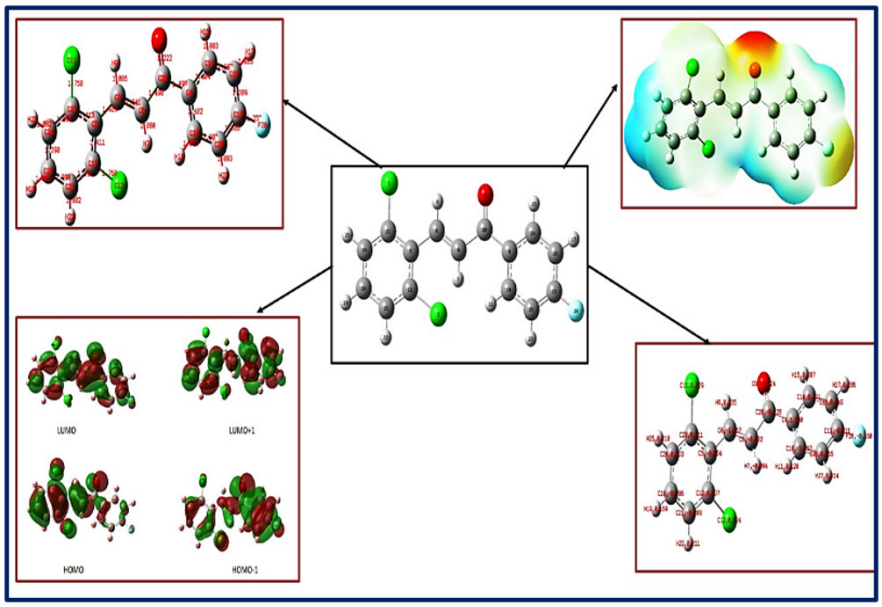
activities like antimicrobial[4,5], antifungal[6] anticancer[7],antileishmanial[8],anti-HIV[9], anti-inflammatory[10], anti-tuberculosis[11], anticonvulsant[12], ant-viral[13], anti-oxidant[14], anti-diabetic[15] etc. Chalcone act as a unique template for synthesis of different heterocyclic like Pyrazoline, Oxazolines, pyrimidines etc.



Graphical Abstract

Density Functional Theory has been very popular in describing the structural and electronic properties of atoms and molecules. The main objective of this paper to synthesized title compound and study their experimental and computational investigation on the Molecular structure, vibrational spectra, and electronic properties. We have synthesized of 2E)-3-(2, 6-dichlorophenyl)-1-(4-Fluoro)-prop-2-en-1-one by Claisen-Schmidt condensation and study their molecular structure, and Vibrational Frequencies investigation by DFT at B3LYP/6-311++G(d,p) level, In addition to this FMOs, ionization potential, electronegativity, global Electrophilicity index, chemical potential were studied by using a 6-311++G (d, p) basis set.

Experimental

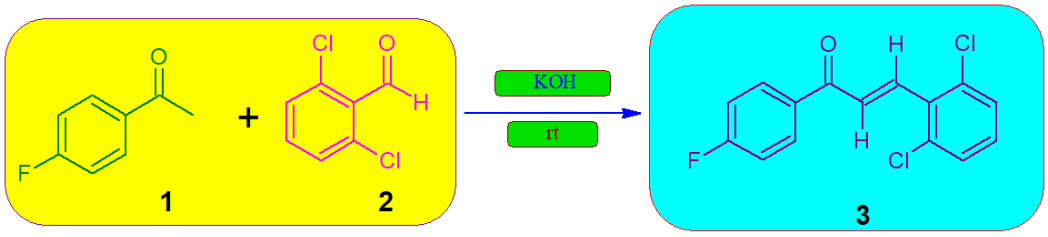
Material and Physical Measurement

The Chemicals used for synthesis are of AR grade. Melting point of the compound was determined in an open capillaries and uncorrected. FTIR spectrum of title compound was recorded on Shimadzu spectrometer using KBr pellets. The 1H NMR was recorded on Brucker Avance 500 MHZ spectrometer using TMS as an internal standard. Reaction is monitored by thin layer chromatography by using n-hexane and ethyl acetate solvent system.

Synthesis of (2E) -3-(2, 6-dichlorophenyl) -1-(4-Fuoro)-prop-2-en-1-one

The 4-Fluoroacetophenone (0.01 mole) and 2, 6 dichloro benzaldehyde (0.01 mole) were dissolved in ethyl alcohol and 5 ml of KOH (20%) was added drop wise to the solution with stirring at room temperature. The completion of the reaction was monitored by TLC. After completion of reaction, reaction mixture poured into crushed ice and acidified with dil. HCl. The solid compound obtained was filtered, dried and recrystallized from ethyl alcohol.

Yield: 87%, FT-IR (KBr,cm-1): 3076 (aromatic C-H), 2839 (C-H), 1664 (C=O), 1602 (C=C), 1508 (aromatic C=C), ; 1H NMR (500 MHz,CDCl3, δ/ppm): 8.05 (d, J= 8.5 Hz.2H), 7.84 (d,J = 16 Hz,1H), 7.63(d, J =16 Hz,1H), 7.387 (d,J =8 Hz,2H), 7.170-7.237 (m,3H).



Scheme 1 Synthesis of (2E) -3-(2, 6-dichlorophenyl) -1-(4-4-Fluoro) -prop-2-en-1-one

Computational details

The Density functional theory (DFT) calculations were performed on an Intel (R) Core (TM) i7 personal computer using Gaussian -03 program package.[17] The geometry of the title compound was optimized by DFT /B3LYF method with 6-311++G (d, p) basis set level.[18-20] To explore the electronic properties, the theoretical UV-Visible spectra have been investigated by the TD-DFT method with a 6-311++G (d, p) basis in the gas phase.

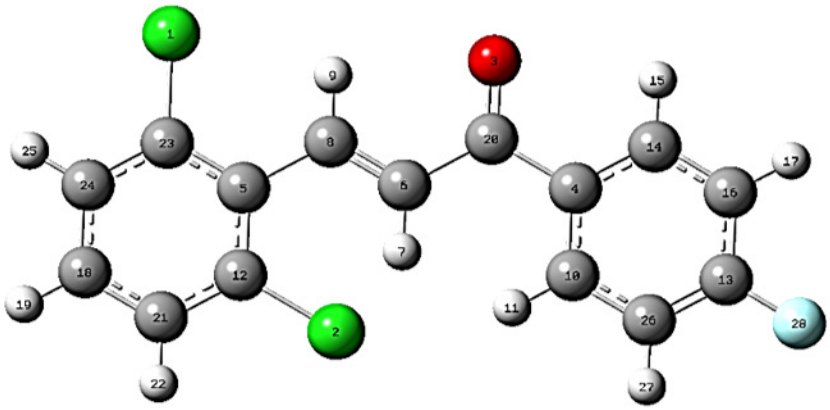


Fig. 1: Optimized structure of title compound

Results and Discussion

Molecular Geometry

The optimize structure of the title compound with the labelling of atoms are shown in Fig.1. The molecular structure of the title compound contains two six membered rings in which, one is 2, 6-dichloro substituted ring attach to C=C of enone system (ring B) and another ring is a 4-Fluoro substituted ring attach to carbonyl group (ring A). The α, β-unsaturated ketone is confirmed by the shorter bond length O2-C20 and C6-C8 are found to be 1.223 Å, 1.34 Å respectively. The C 13-F28, Cl1-C23 and Cl2-C12 bond lengths are 1.352 Å, 1.757 Å and 1.759 Å respectively and found within the normal range. All the bond lengths are within the normal range and compared with the previously reported structure.[22-26] The calculated C_{20}-C_6, C_8-C_5 torsion angle is 179.50 confirms the molecule exhibits E configuration, which shows trans geometry.

Vibrational Frequency Assignment

Comparison of vibrational assignment of title compound by Experimental IR spectrum with theoretical IR spectrum. Experimental IR spectrum is recorded in the region of 4000-500 cm^{-1}(Solid phase) and calculated vibrational spectrum in the gas phase. Title compound contains total 28 atoms with 78 fundamental modes of vibration. Theoretical and experimental IR spectrum is shown in Fig 4a and 4b.Carbonyl stretching frequency of alpha beta unsaturated ketone in the range of 1700-1600 cm^{-1}, the experimental carbonyl stretching frequency of title compound 1658 cm^{-1} and theoretically it is 1664 cm^{-1} this confirms presence of carbonyl group,

lower value of IR frequency is due to conjugation of enone system with the aromatic rings. Experimental IR at 1525cm^{-1} and theoretical IR at 1508cm^{-1} is due to the Ar-C=C- stretching vibrations. Out of plane bending vibrations experimentally at 972.12 cm^{-1} and theoretically at 972 cm^{-1} shows trans geometry of alkene. The C-H experimental and theoretical is stretching vibration 3076 cm^{-1} and 3072 cm^{-1} respectively.

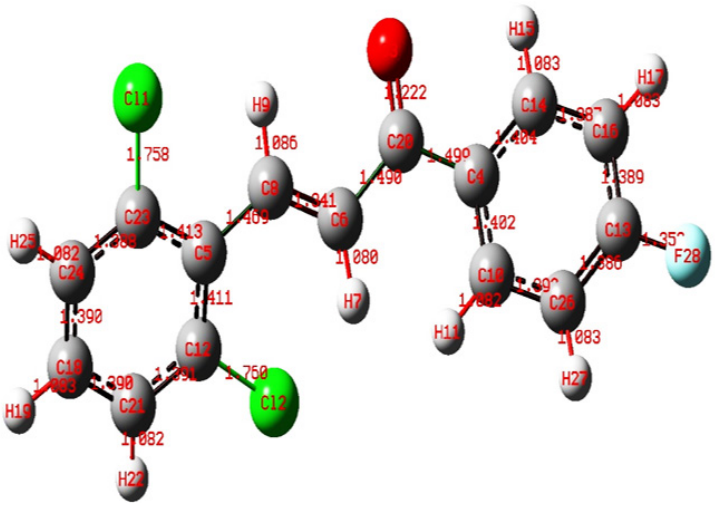
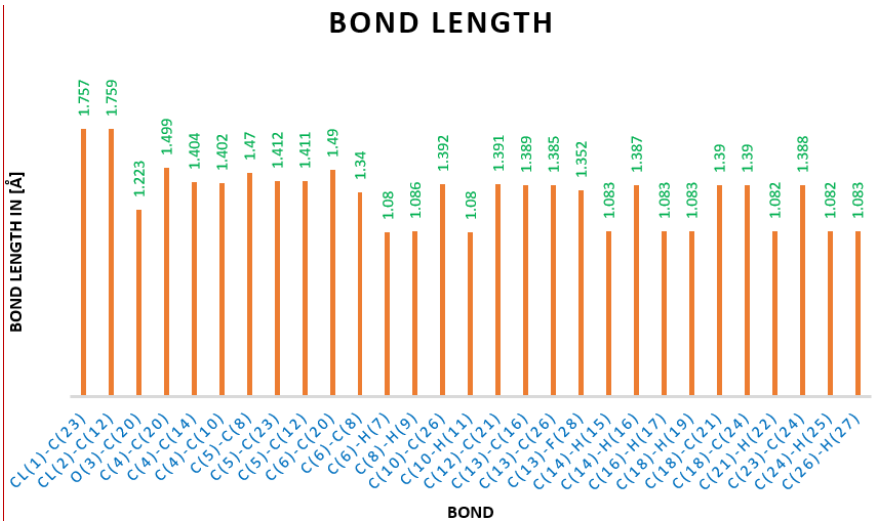


Fig.2: Bond length of the title compound

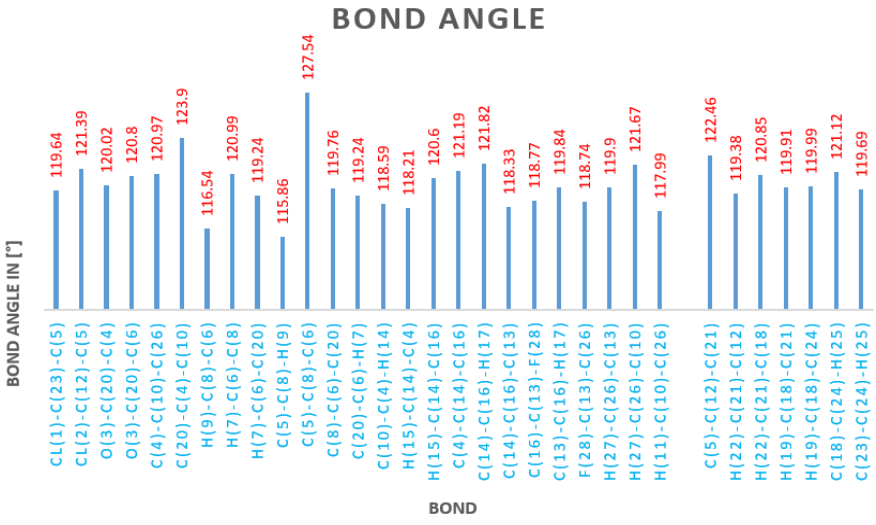
Table 1: The bond length and dihedral angle of title compound calculated at B3LYP/6-311++G (d, p) level

Bond	Bond Length [Å]	Bond	Bond Angle [°]
Cl(1)-C(23)	1.757	Cl(1)-C(23)-C(5)	119.64
Cl(2)-C(12)	1.759	Cl(2)-C(12)-C(5)	121.39
O(3)-C(20)	1.223	O(3)-C(20)-C(4)	120.02
C(4)-C(20)	1.499	O(3)-C(20)-C(6)	120.8
C(4)-C(14)	1.404	C(4)-C(10)-C(26)	120.97
C(4)-C(10)	1.402	C(20)-C(4)-C(10)	123.9
C(5)-C(8)	1.470	H(9)-C(8)-C(6)	116.54
C(5)-C(23)	1.412	H(7)-C(6)-C(8)	120.99
C(5)-C(12)	1.411	H(7)-C(6)-C(20)	119.24
C(6)-C(20)	1.490	C(5)-C(8)-H(9)	115.86
C(6)-C(8)	1.340	C(5)-C(8)-C(6)	127.54
C(6)-H(7)	1.080	C(8)-C(6)-C(20)	119.76
C(8)-H(9)	1.086	C(20)-C(6)-H(7)	119.24
C(10)-C(26)	1.392	C(10)-C(4)-H(14)	118.59
C(10-H(11)	1.080	H(15)-C(14)-C(4)	118.21
C(12)-C(21)	1.391	H(15)-C(14)-C(16)	120.60
C(13)-C(16)	1.389	C(4)-C(14)-C(16)	121.19
C(13)-C(26)	1.385	C(14)-C(16)-H(17)	121.82
C(13)-F(28)	1.352	C(14)-C(16)-C(13)	118.33
C(14)-H(15)	1.083	C(16)-C(13)-F(28)	118.77
C(14)-H(16)	1.387	C(13)-C(16)-H(17)	119.84
C(16)-H(17)	1.083	F(28)-C(13)-C(26)	118.74

C(14)-H(16)	1.387	C(13)-C(16)-H(17)	119.84
C(16)-H(17)	1.083	F(28)-C(13)-C(26)	118.74
C(18)-H(19)	1.083	H(27)-C(26)-C(13)	119.90
C(18)-C(21)	1.390	H(27)-C(26)-C(10)	121.67
C(18)-C(24)	1.390	H(11)-C(10)-C(26)	117.99
C(21)-H(22)	1.082	C(5)-C(12)-C(21)	122.46
C(23)-C(24)	1.388	H(22)-C(21)-C(12)	119.38
C(24)-H(25)	1.082	H(22)-C(21)-C(18)	120.85
C(26)-H(27)	1.083	H(19)-C(18)-C(21)	119.91
		H(19)-C(18)-C(24)	119.99
		C(18)-C(24)-H(25)	121.12
		C(23)-C(24)-H(25)	119.69

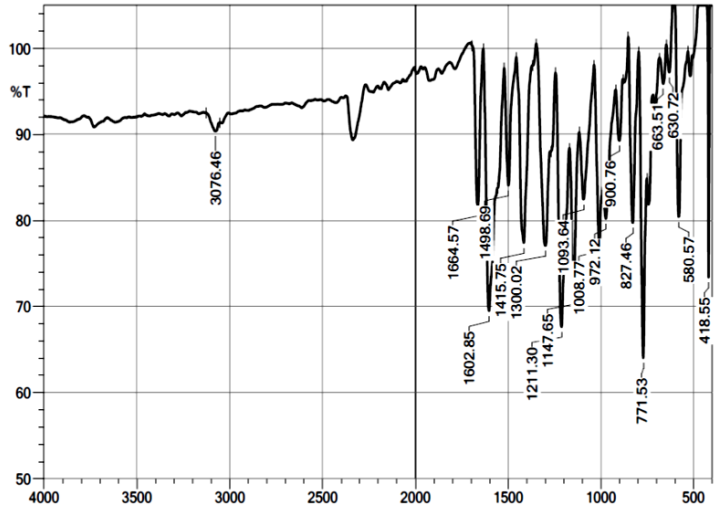


(a)

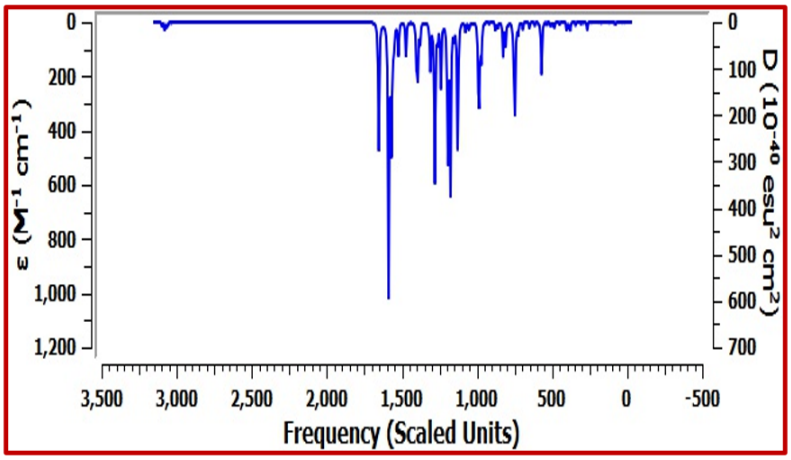


(b)

Fig.3: a) The Graphical representation of bond length and b) Bond Angle



(a)



(b)

Fig. 4: a) Experimental FT-IR spectrum and b) Simulated IR spectrum of title compound

Table 2: Selected Experimental and theoretical vibrational assignments of title compound

Selected mode no	Calculated (Scaled) frequencies in cm^{-1}	Calculated IR intensity	Experimental Frequencies cm^{-1}	Assignment
78	3104	4.25	-	υ_{sym} (10)C-(11)H ring b+ υ_{sym} (6)C-(7)H(C=C)
77	3087	2.29	-	υ_{sym}CH (Ring a)
76	3085	5.50	-	υ_{sym} CH (Ring b)
75	3083	0.86	-	υ_{sym} CH (Ring b)
74	3082	0.24	-	υ_{asymm} (Ring a)
73	3072	0.189	3076	υ_{asymm} (Ring b) CH+ υ_{sym} (6)C-(7)H(C=C)
72	3070	5.17	-	υ_{asymm} (Ring b)

71	3061	2.64	-	υ_{asymm} (Ring a)
70	3042	1.69	-	(8)C- (9)H(C=C)
69	1656	136.31	1664.57	υ C=O
68	1590	289.29	1602.85	υ C=C,C=O
67	1572	129.83	-	υ C=C and CH (Ring b)
66	1560	19.88	-	υ C=C and CH (Ring b)
65	1554	18.02	-	υ C=C and CH (Ring a)
64	1525	33.85	1508	υ C=C and CH (Ring a)
63	1475	35.93	1498.69	υ C=C and CH (Ring b)
62	1405	42.57	1415.75	υ C=C and CH (Ring a)
60	1381	20.89	-	υ C=C and CH (Ring b)
59	1312	49.65	1300.02	υ C=C
58	1289	17.59	-	υ C=C and CH (Ring b)
55	1242	67.61	-	υ C=C (Ring a)
46	1048	2.56	1093.64	υ C=C and CH (Ring a)
45	992	53.00	1008.77	υ C=C and CH (Ring b)
43	972	39.33	972.12	υ γ CH (C=C)
40	921	1.54	900.76	υ CH (Ring a)
39	879	8.54	-	υ CH(C=C)
36	827	36.16	827.46	υ CH (Ring a)
35	810	23.98	-	υ C-(28)F
34	794	1.83	-	υ CH (Ring b)
33	760	3.36	771.53	υ CH (Ring b)
31	748	91.73	-	υ C-(1)Cl

v- stretching; asym-asymmetric; sym-symmetric; def-deformation; β-In-plane bending; γ-out of plane bending, ρ-rocking, Γ-torsion

UV-Vis Spectra Study and Global Chemical Reactivity Parameters

The absorption energies (λ in nm), oscillator strength (*f*), and electronic transitions of the title compound have been computed at the TD-DFT B3LYP/6-311++G (d, p) level of theory for optimized geometry. To study the effect of solvent on the wavelength of absorption, TD-DFT calculation, perform in both gas and DCM solvent. The calculated electronic transitions of high oscillatory strength, wavelength are given in Table 3. The first singlet state (S1) is found to be at 366 nm in DCM (Fig.5) and 378 nm in the gas phase (Fig. 5). The second singlet excited state (S2) is present at 326 nm (DCM) and 314 nm (gas phase). The third singlet excited state (S3) is present at 322 nm (DCM) and 311 nm (gas phase). The Simulated spectrum (Gas and DCM) is illustrated in Fig.5 The assigned bands were characterized by ($n\rightarrow\varpi^*$) and ($\varpi\rightarrow\varpi^*$) transitions.

Table 3: Absorption energies (λ in nm), oscillator strength (*f*), and transitions of title compound computed at TD-DFT B3LYP/6-311++G (d, p) level of theory

State	DCM				Gas Phase			
	Config	**f**	**λ, nm**	**Excitation energy (eV)**	**Config**	**f**	**λ, nm**	**Excitation energy (eV)**
I	72 -> 76 73 -> 76 75 -> 76	0.0234	366	3.3863	72 -> 76 74 -> 76 75 -> 76	0.0066	378	3.2723

II	72 -> 76	0.6083	326	3.7921	74 -> 76	0.5315	314	3.9478
	73 -> 76				75 -> 76			
	74 -> 76				-			
	75 -> 76				-			
III	74 -> 76	0.0703	322	3.8491	72 -> 76	0.0560	311	3.9791
	75 -> 76				73 -> 76			
	75 -> 78				74 -> 76			
	-				75 -> 76			
	-				75 -> 78			
IV	71 -> 76	0.0523	294	4.2073	71 -> 76	0.0272	291	4.2563
	72 -> 76				72 -> 76			
	73 -> 76				73 -> 76			
	75 -> 76				74 -> 76			
	-				75 -> 76			
V	71 -> 76	0.0373	286	4.3229	71 -> 76	0.0165	281	4.4066
	72 -> 76				72 -> 76			
	73 -> 76				74 -> 79			
	73 -> 79				-			

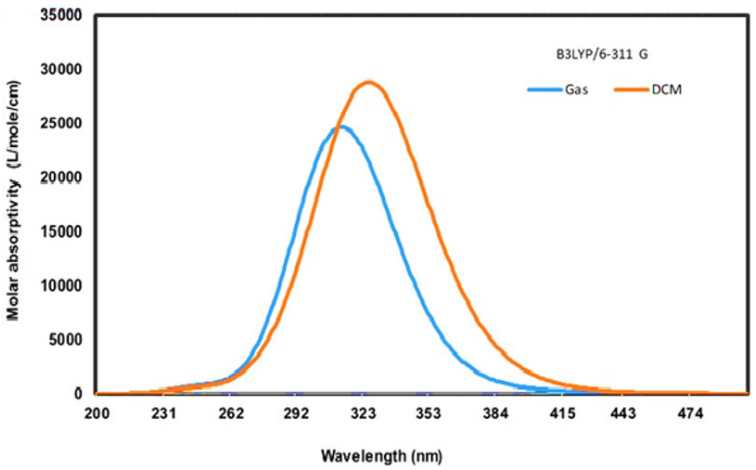


Fig. 5: The Simulated UV-visible absorption spectra for the title compound in vacuum and DCM solvent computed at B3LYP/6-311++G (d, p) level of theory

Global Chemical Reactivity Descriptors

The highest molecular orbital and lowest molecular orbital are called frontier molecular orbitals. The HOMO-LUMO energy value and energy gap values for title compound were computed by the TD-DFT method at B3LYP/6-311G (d, p) basis set in gas phase. HOMO-LUMO plot of title compound is shown in Fig.6 the computed gas phase HOMO and LUMO energies are -7.2328 eV and -2.7225 eV respectively. Whereas the energy gap of title compound is 4.5103eV. From the HOMO-LUMO energies various chemical reactivity parameters have been derived. The Ionization potential (I), Electron Affinity (A), Chemical hardness (η), Chemical softness (S), Electronic chemical potential (μ), Global Electrophilicity index (ω) parameters were calculated based on Koopman's theorem[26] equation 1-4.[27-30] The HOMO-LUMO energies and global reactivity parameters are listed in table 5.The global hardness (η) of 2.2551eV, Chemical Softness (S) 0.4434eV, chemical potential (μ) -4.9777 eV, electrophilicity Index (ω) 4.8554eV suggest the good stability of the compound.

$\eta = ½ (I - A)$ ...(1) $\mu = -½ (I+A)$ …(3)

$S = 1/\eta$ ...(2) $\omega = \mu 2 / 2\eta$ …(4)

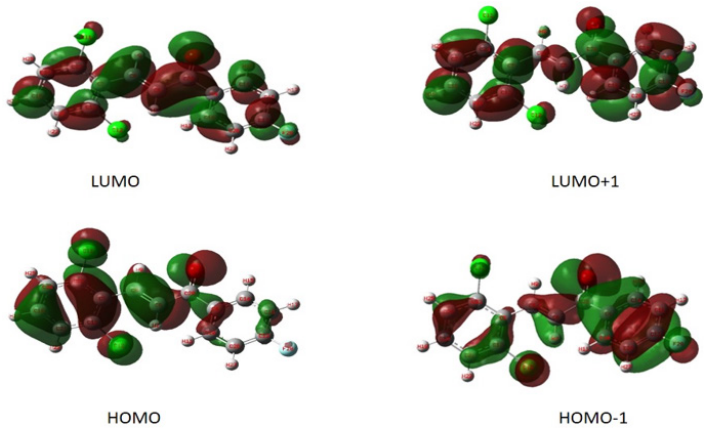


Fig.6: Frontier molecular orbitals of title Molecule

Table 4: Global chemical reactivity indices calculated at B3LYP/6-311G++(d,p) level

Parameters	B3LYP/6-311++G(d,p)
E_{LUMO} (eV)	-2.7225 eV
E_{HOMO} (eV)	-7.2328 eV
$\Delta E = E_{LUMO}-E_{HOMO}$ (eV)	4.5103 eV
Electron affinity (A)	2.7225 eV
Ionization Energy (I)	7.2328 eV
Global Hardness (η)	2.2551 eV
Chemical Softness (S)	0.4434 eV
Electronic chemical potential (μ)	-4.9777 eV
Global electrophilicity Index (ω)	4.8554 eV

Mulliken Atomic Charges

The Mulliken atomic charges play an important role to know the chemical reactivity of compounds. The Mulliken atomic charges calculated and reported of title compound is shown in Table 5. As indicated in table 5 The C_4 atom carries the larges positive charge 1.657 among other carbon atoms and therefore expected to be the site for nucleophilic attack in title compound, whereas C_8 and C_{10} carries higher negative charge -1.225 and -1.633 respectively in all carbon atoms. The Molecular electrostatic potential plot is shown in Fig.8, this gives information about the chemical reactivity of sites. The dipole moment of the title compound is 3.9 Debye indicates polar nature.

Antimicrobial activity of the title compound

The newly synthesized (2E)-3-(2,6-dichlorophenyl)-1-(4-4-Fluoro)-prop-2-en-1-one were screened for their antimicrobial activities *in vitro* against *staphylococcus aureus, bacillus subtillis,Escheria coli salmonella Typhi* pathogenic bacteria and three fungi *Aspergillus Niger, Aspergillus flavus candida albicans*. Antimicrobial activity of title compound was tested using the agar diffusion method.[32] The antimicrobial activity data of synthesized compounds, from the result the title compound shows moderate activity against all organisms.

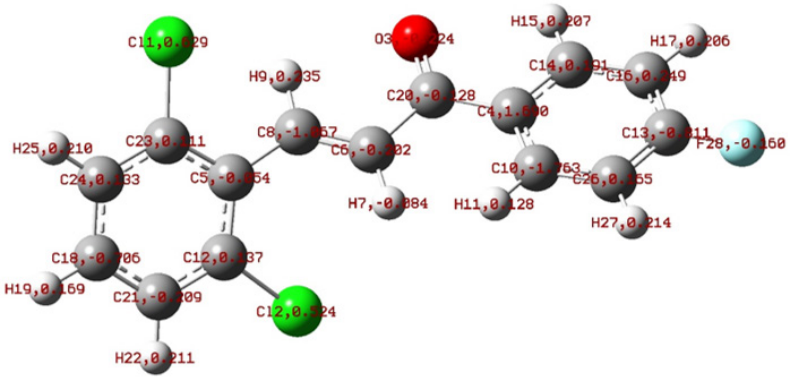


Fig. 7: Mulliken atomic charges representation

Table 5: Mulliken atomic charges of Title compound at B3LYP/6-311++G (d, p) level

Atom	Charge	Atom	Charge
1Cl	0.635	15 H	0.208
2 Cl	0.543	16 C	-0.008
3 O	-0.223	17 H	0.204
4 C	1.657	18 C	-0.667
5 C	0.333	19 H	0.170
6 C	-0.317	20 C	-0.222
7 H	-0.058	21 C	-0.151
8 C	-1.225	22 H	0.211
9 H	0.240	23 C	-0.172
10 C	-1.633	24 C	0.001
11 H	0.101	25 H	0.212
12 C	0.324	26 C	-0.144
13 C	-0.618	27 H	0.214
14 C	0.548	28 F	-0.164

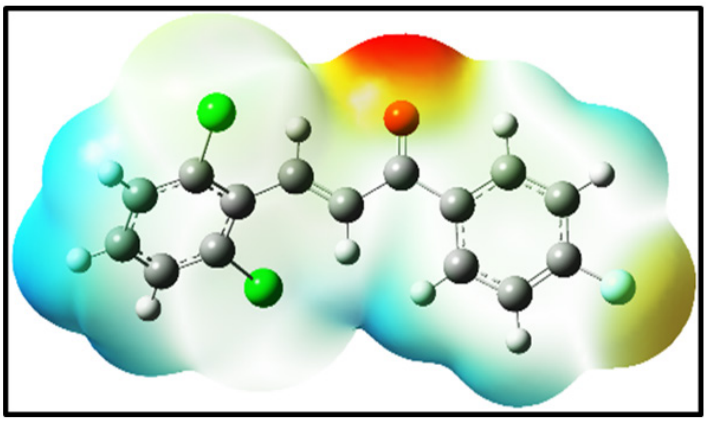


Fig.8: Molecular Electrostatic potential plot of the title compound

Table 6: Antimicrobial activity

Product	Bacteria				Fungi		
	Ec	Bs	St	Sa	An	Af	Ca
Compound	11(25)	12(25)	10(25)	09(25)	08(25)	12(25)	09(25)
Penicillin	15(25)	17(25)	13(25)	13(25)	NA	NA	NA
Nystatin	NA	NA	NA	NA	16(25)	14(25)	13(25)

Zone of inhibition is expressed in mm, Ec-*Escherichia coli*, An-*Aspergillus niger,* Sa-*Staphylococcus aureus*, Af-*Aspergillus flavus*, Bs- *Bacillus subtillis-Salmonella Typhi*, Ca- *Candida albicans*, -- No activity, NA-Not Applicable

Conclusion

(2E)-3-(2, 6-dichlorophenyl)-1-(4-4-Fluoro)-prop-2-en-1-one synthesized by claisen-Schimdt condensation and spectroscopic characterization by using FT-IR and 1H NMR and study of molecular structure, bond length, bond angle etc. by using Density Functional Theory B3LYP/6-311++G(d,p) basis set. It was found that experimental vibrational frequencies show good agreement with the calculated vibrational frequencies. The dipole moment of title compound is 3.9036 Debye shows polar nature. All hydrogen's are electropositive except H_7 and C_{10} carries a higher negative charge. In addition to this energy of HOMO-LUMO, thermodynamic properties like Enthalpy, Entropy, and Polarizability are calculated. From the DFT study gives information about the reactivity of molecule. The title compound shows moderate activity against all bacteria and fungi.

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Conflict of interest

The author declares that they have no conflict of interest.

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