Computational and Spectral Discussion of Some Substituted Chalcone Derivatives

Velayutham Shanmuga Vadivoo 1, Chithathoor Venugopal Mythili 1*, Ramalingam Balachander 2, Natarajan Vijayalakshmi 3, Parimalaselvam Vijaya 1

1 Department of Chemistry, Rani Anna Govt. College for Women (Affiliated to Manonmani Sundaranar University), Palayapettai 627 008, Tirunelveli, Tamil Nadu, India
2 Department of Chemistry, Periyar Arts College, Cuddalore 607 001, Tamil Nadu, India
3 Department of Chemistry, Shree Raghavendra Arts and Science College, Keezhamoongiladi 608 602, Chidambaram, Tamil Nadu, India
* Correspondence: vsvchemresearch@gmail.com (C.V.M.);
Scopus Author ID 8886486400

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Abstract: The substituted chalcone derivatives 1–7 have been synthesized, and spectroscopic characterization were done as done using the experimental FT-IR, UV-Vis, GC-MS, 1D NMR spectroscopy. The favored conformation of substituted chalcone 3 was predicted theoretically by geometry optimization structure selected geometrical parameters and molecular properties such as NBO, AIM, HOMO-LUMO, MEP surface, and atomic charges were derived from optimized structures. The 1H and 13C NMR spectral data had been additionally computed using the Gaussian-09 package and compared with the experimental values. The antibacterial and antifungal activity was derived by the disc diffusion method.

Keywords: computation; synthesis; spectral; chalcones; conformations; biological activity.

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1. Introduction

Chalcones are open-chain flavonoids with two aromatic rings attached by carbonyl groups and two α,β-unsaturated carbon atoms [1–6]. They are well-known intermediates for synthesizing different types of heterocyclic compounds such as isoxazolines [7], pyrazolines [8–13], pyrazoles [14], pyridines [15], cyclohexenones [16], and oxadiazole [17] derivatives which could be potential drug candidates. It possesses acceptor and donor groups, which enhance their importance in various fields. Chalcone derivatives are promising compounds to be developed as their chromophore absorbs in the UV region from Sunscreen Agent. The nonlinear optical (NLO) properties of conjugated organic compounds have been the major focus of various computational and experimental studies because of their promising applications in photonics and optoelectronics, integrated optics, photophysical, high-speed optical communications, optical data processing, and storage [18,19]. The chalcone compounds have high significance because of their excellent NLO properties [20]. Chalcones are intramolecular charge transfer molecules, which allow one to design them based on the above design criteria. Chalcones are well known for their excellent blue-light transmittance and high second harmonic generation (SHG) conversion efficiency [21]. These chalcones crystallize in a non-centrosymmetric crystal structure and provide a necessary configuration for NLO activity with two planar benzene rings connected through a conjugated double bond [22-24]. Most of the
work reported on these chalcones is about SHG and hirshfeld surface analysis (HAS) [25-27]. The molecule must have an π-electron backbone connected to acceptors/ donors groups [28,29], commonly designated lateral substituents. The size of the molecule could also be an essential parameter to improve the NLO response, but if one considers this as a blind parameter than the shortest molecules will always be at a disadvantage against the biggest ones. Indeed, if the dimensions of the -electron spine will increase, the NLO response commonly increases a great-linear feature [30,31]. Despite that, molecules with a short-electron spine period could also reap desirable NLO responses, depending on the kind and function of the lateral substituents used [32–36]. Chalcone derivatives are promising compounds to be developed as their chromophore absorbs in the UV region from Sunscreen Agent, photoprotective and antioxidant properties [37-40]. Generally, chalcones are pharmacological activities such as anti-inflammatory, antibacterial, anticancer [41], antimalarial, antiproliferative [42], antifungal, antiviral, antioxidant, antineoplastic [43]. Free radical scavenging properties of phenol groups of chalcones increased the interest in the consumption of plants that included chalcones. Being the precursors of all the other flavonoid groups, chalcones are very important biosynthetic compounds. Much research work has been done on the synthesis and reactions of the chalcones.

The present investigation focuses on the synthesis and theoretical investigation of the molecular structure, charges, NBO, and AIM analysis of some known substituted chalcones. HOMO-LUMO energies, MEP surface dipole moment, polarizability, and first hyperpolarizability were also determined by DFT method and analyzed.

2. Materials and Methods

2.1. Synthesis of substituted chalcones 1–7.

Substituted acetophenone (0.01 mol) and 4-methoxybenzaldehyde (0.01 mol) were dissolved in ethanol. The ethanolic reaction mixture is poured into an RB flask [44]. The mixture is kept in an ice bath and stirred using a magnetic stirrer. Then 10 mL of 2 N NaOH solution is added dropwise to the reaction mixture and stirred vigorously for 30 min. After vigorous stirring, the reaction mixture is transferred to a beaker and kept in a refrigerator overnight. Then the reaction mixture is neutralized using HCl in the cold condition where precipitation occurred. On filtering off, the yellow color crude chalcone is obtained and dried. The crude is purified using thin-layer chromatography, and it can be performed on an aluminum plate pre-coated with silica gel-G using ethyl acetate and n-hexane (7:3) (Rf = 0.7) as the solvent, and the spot was exposed to iodine vapor. The pure product was recrystallized from ethanol. The physical data are: 1. m.p. 110 °C, yield 90%, GC-MS: 239.4 [M+]; 2. m.p. 115 °C, yield 89%, GC-MS: 253.3 [M+]; 3. m.p. 119 °C, yield 85%, GC-MS: 267.5 [M+], 268.4 [M+1]; 4. m.p. 132 °C, yield 90%, GC-MS: 257.6 [M+], 258.2 [M+2]; 5. m.p. 135 °C, yield 90%, GC-MS: 274.2 [M+], 275.5 [M+2]; 6. m.p. 128 °C, yield 90%, GC-MS: 317.4 [M+1], 318.4 [M+2]; 7. m.p. 144 °C, yield 85%, GC-MS: 284.3 [M+], 285.3[M+2].

2.2. Spectral measurements.

The 1H NMR (400 MHz) and 13C NMR (100 MHz) had been recorded at room temperature on Bruker 400 MHz instrument compounds dissolved for chloroform-d6. The mass spectra were performed using Varian Saturn 2200 GC-MS spectrometers.
FT-IR spectrometer and the wavenumbers are given in cm\(^{-1}\). The UV-visible spectra of the chalcones 1–7 are recorded in Shimadzu-UV-1800-UV-Visible spectrophotometer using N,N-dimethylformamide as solvent at ambient room temperature.

2.3. Computational study.

Geometry optimizations were carried out according to density functional theory using B3LYP/6-31G(d,p) basis set [45] in the Gaussian-09 package. The polarizabilities and hyperpolarizabilities have been derived from the DFT optimized structure by using finite discipline technique using the B3LYP/6-31G* basis set, while the NBO calculations were carried out using the premise set B3LYP/6-311+G(d,p) available in Gaussian-09 and AIM calculations were done using B3LYP/6-31G(d,p) basis set.

3. Results and Discussion

\((E)\)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one 1, \((E)\)-1-(4-methoxyphenyl)-3-p-tolylprop-2-en-1-one 2, \((E)\)-1,3-bis(4-methoxyphenyl)prop-2-en-1-one 3, \((E)\)-3-(4-fluorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 4, \((E)\)-3-(4-chlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 5, \((E)\)-3-(4-bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 6 and \((E)\)-1-(4-methoxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one 7 were synthesized according to the Scheme 1 and characterized by GC-MS, IR, UV-Vis, \(^1\)H and \(^{13}\)C NMR spectra. The labeling of the atoms followed in the present study was also indicated in the Scheme 1.

![Scheme 1](image)

**Scheme 1.** Steps involved in the synthesis of chalcones 1–7.

3.1. IR spectra.

The intense peaks around 1664 cm\(^{-1}\) in the IR spectra of 1–7 are presented to \(\nu_C=O\) of the carbonyl group. The aromatic \(\nu_C=C\) stretching vibrations are observed around 3129 cm\(^{-1}\), and the stretching vibrations of the aromatic –CH= out-of-plane bending vibrations have appeared around 854 cm\(^{-1}\). The \(\alpha,\beta\)-unsaturated –C=C– chain are found to be 1212 cm\(^{-1}\). Compound 7 peaks for \(\nu_{NO2}\) group are observed in regions 1505 and 1480 cm\(^{-1}\). The sharp peaks region 1086 cm\(^{-1}\) are attributed to \(\nu_C-O\) mode. The appearance of peaks around 1268 cm\(^{-1}\) is due to the presence of asymmetric C–O–C stretching vibration. The intense high peaks around 612 to 543 cm\(^{-1}\) are assigned to C–X (X= F\(_2\), Cl, and Br) stretching vibration [46,47]. The remaining IR spectral data of 1–7 are listed in Table 1.

| Assignments | 1  | 2  | 3  | 4  | 5  | 6  | 7  |
|-------------|----|----|----|----|----|----|----|
| \(\nu_C=O\) | 1660 | 1654 | 1658 | 1655 | 1659 | 1664 | 1657 |
| \(\nu_C=C\) | 3045 2954 | 3028 2989 | 3073 2969 | 3127 | 3025 2935 | 3129 | 2980 |
3.2. Electronic spectral studies.

The ultraviolet absorption spectra were recorded for all the synthesized chalcones 1–7 in dimethylformamide region 260–400 nm. The maximum absorption values around 347, 348, 358, 360, 363, 350, and 389 nm due to n-π* transition and 280, 286, 275, 260, 290, 273 and 297 nm due to π-π* transition, which may be attributed the excitation in the C=O and –C=C– group [45]. The higher λmax is observed for 7 when compared to the other chalcones 1–6 due to the presence of NO₂ moiety. UV-visible spectra of 3, 4, and 7 are shown in Figs. 1-3.

![Figure 1. UV-Vis spectrum of 3.](image1)

![Figure 2. UV-Vis spectrum of 4.](image2)

![Figure 3. UV-Vis spectrum of 7.](image3)

3.3. 1H NMR spectral analysis.

(E)-3-(4-Fluorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 4, the signals in the 1H NMR spectrum was assigned based on these positions, integrals, and multiplicities.

(E)-3-(4-Fluorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 4, the signals in the 1H NMR spectrum was assigned based on these positions, integrals, and multiplicities.
high-frequency doublet at 8.04 ppm is assigned to H–11 and H–15 protons (meta position with respect methoxy and ortho position concerning carbonyl group with coupling constant 8.8 Hz). The doublet of the doublet peak observed at 7.63 ppm is assigned to H–5 and H–9 protons (integrated corresponding to two protons coupling constant 8.4 Hz). The special category of fluorine substituted in aromatic rings is observed in $^1$H NMR spectra as a doublet of the doublet. The remaining aromatic ring protons that appeared at 7.11 and 6.99 ppm are represented H–6/H–8 and H–12/H–14. The two doublets seem at 7.76, and 7.47 ppm (each doublet for one proton) are assigned to $\alpha$ and $\beta$ hydrogen of chalcone moiety at H–3 and H–2 protons with a coupling constant of 15.6 Hz, which is characterized to geminal coupling constant of trans configuration. The $^{13}$C NMR spectrum less intense peak observed at 187.5 ppm is assigned to carbonyl carbon C–1. There are four ipso carbons present in this molecule, and their peaks are observed in the spectra. A low-frequency signal at 123.71 ppm is assigned to the quaternary carbon C–4 since it is para concerning the electron-withdrawing fluorine group. The signal at 141.75 ppm is assigned to the ipso carbon C–7, attached to the fluorine atom F–19. The two signals at 130.27 and 163.31 ppm are due to C–10, which is linked to carbonyl carbon C–1 and C–13, respectively. The remaining aromatic ring carbons appeared at 114.04, 130.96, 130.63, and 131.83 ppm, respectively. In a similar manner, assignments were done for other chalcone derivatives 1–3 and 5–7. The $^1$H and $^{13}$C chemical shift values are obtained in Tables 2 and 3, the $^1$H and $^{13}$C NMR spectra of 4 as shown in Figs. 4 and 5, respectively.

Values within parentheses are the observed coupling constants.

### Table 2. $^1$H NMR chemical shifts (ppm) of 1–7.

| Compds. | H–2 | H–3 | H–5/H–9 | H–6/H–8 | H–11/H–15 | H–12/H–14 | H–18 | H–19 |
|---------|-----|-----|---------|---------|-----------|-----------|------|------|
| 1       | 7.46 | 7.83 (d, 15.6 Hz) | 7.51 | 6.74 (d, 15.0 Hz) | 8.04 | 7.04 | 5.56 | s   |
| 2       | 7.49 | 7.79 (d, 15.6 Hz) | 7.53 | 6.98 (d, 8.8 Hz) | 8.04 | 7.22 (d, 8.0 Hz) | 3.89 | (s) |
| 3       | 7.77 | 7.83 | 7.81 | 7.02 (d, 8.8 Hz) | 8.14 | 7.08 (d, 7.8 Hz) | 3.87 | (s) |
| 4       | 7.76 | 7.47 | 7.63 (d, 8.8 Hz) | 6.99 (d, 8.0 Hz) | 8.04 | 7.11 | 3.90 | (s) |
| 5       | 7.83 | 7.95 | 7.66 (m) | 7.66 (m) | 8.16 (d, 9.2 Hz) | 7.09 (d, 8.8 Hz) | 3.87 | (s) |
| 6       | 8.74 | 7.43 | 7.60 | 7.67 | 7.67 | 7.04 (d, 8.8 Hz) | 3.67 | (s) |
| 7       | 7.67 | 7.09 | 7.69 (d, 8.0 Hz) | 8.17 (d, 8.0 Hz) | 7.21 | 7.09 (d, 8.4 Hz) | 3.87 | (s) |

### Table 3. $^{13}$C NMR chemical shifts (ppm) of 1–7.

| Compds. | C–1 | C–2 | C–3 | C–4 | C–5/ C–9 | C–6/ C–8 | C–10 | C–11/ C–15 | C–12/ C–14 | C–7 | C–13 | C–18/ C–14 |
|---------|-----|-----|-----|-----|---------|---------|------|-----------|------------|------|------|-----------|
| 1       | 185.73 | 115.47 | 138.71 | 126.73 | 110.67 | 130.27 | 123.73 | 112.96 | 130.65 | 130.33 | 158.71 | 55.41 |
| 2       | 186.83 | 118.17 | 140.73 | 129.33 | 112.97 | 130.45 | 126.33 | 114.01 | 130.85 | 130.61 | 161.73 | 55.56 |
| 3       | 187.36 | 119.46 | 143.14 | 127.38 | 113.95 | 130.60 | 127.38 | 114.37 | 130.74 | 161.20 | 163.06 | 55.50/ 55.33 |
| 4       | 187.35 | 122.81 | 134.05 | 123.71 | 130.96 | 114.04 | 130.27 | 131.83 | 130.63 | 141.75 | 163.31 | 55.56 |
| 5       | 184.23 | 121.51 | 141.75 | 134.05 | 130.63 | 130.27 | 123.71 | 130.96 | 114.04 | 134.05 | 163.30 | 55.47 |
| 6       | 187.33 | 121.73 | 142.83 | 134.11 | 130.30 | 130.17 | 122.89 | 130.45 | 113.86 | 134.00 | 163.05 | 55.73 |
| 7       | 187.44 | 121.21 | 143.62 | 130.33 | 130.49 | 106.37 | 139.60 | 130.90 | 113.96 | 153.08 | 163.17 | 56.09 |

### 3.4. Conformational analysis.

There are three possible conformations for the chalcone 3, as shown in Fig. 6. In conformation A, both methoxy methyl moiety is syn to $\alpha$, $\beta$-unsaturated carbonyl group C=O chain, whereas, in B, it is anti. The conformation C, one methoxy methyl is syn another methoxy methyl is anti to the carbonyl carbon. Theoretical study [relative energies are 0.22
(A), 0.39 (B), and 0.00 (C) kcal mol\(^{-1}\) predicts the favored conformation as C only for the chalcone 3.

Figure 4. \(^{1}H\) NMR spectrum of 4.

Figure 5. \(^{13}C\) NMR spectrum of 4.

Figure 6. Possible conformations of 3.
3.5. Molecular properties.

3.5.1. Geometric parameters.

The selected bond length, bond angle, and torsional angle values are derived from the corresponding optimized structures 1–7 are given in Table 4. The torsional angle C11–C10–C1–C2 in chalcone 3 (−0.35°) differs from other chalcones 1–7 (~0.30°) indicating that the α,β-unsaturated –C=C– chain slightly distorted from the other chalcones. Further, the nitro substituted chalcone torsional angle is a slight deviation from the other chalcones 1–6. The optimized structures of chalcones 1–7 are shown in Fig. 7.

| Table 4. Selected geometric parameters [bond lengths (Å), bond angles (°) and torsional angles (°)] in 1–7. |
|---------------------------------------------------------------|
| **Geometric parameters** | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| **Bond lengths** | | | | | | | |
| C1-O16 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 | 1.22 |
| C1-C2 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 |
| C2-C3 | 1.34 | 1.34 | 1.34 | 1.34 | 1.34 | 1.34 | 1.34 |
| C4-C5 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 |
| C5-C6 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 |
| C7-C8 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 | 1.48 |
| C8-C9 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 |
| C1-C10 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 |
| C10-C11 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 |
| C11-C12 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 | 1.50 |
| C12-C13 | 1.41 | 1.41 | 1.41 | 1.41 | 1.41 | 1.41 | 1.41 |
| C13-O17 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 | 1.39 |
| O17-C18 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 |
| C13-C14 | 1.35 | 1.35 | 1.35 | 1.35 | 1.35 | 1.35 | 1.35 |
| C14-C15 | 1.42 | 1.42 | 1.42 | 1.42 | 1.42 | 1.42 | 1.42 |
| C15-C10 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 | 1.40 |
| N19-O20/21 | – | – | – | – | – | – | 1.23/ |
| **Bond angles** | | | | | | | 1.23 |
| O16-C1-C2 | 120.92 | 120.92 | 120.92 | 120.92 | 120.92 | 120.92 | 120.92 |
| O16-C1-C10 | 119.14 | 119.14 | 119.14 | 119.14 | 119.14 | 119.14 | 119.14 |
| C1-C2-C3 | 120.37 | 120.37 | 120.37 | 120.37 | 120.37 | 120.37 | 120.37 |
| C2-C3-H3 | 116.09 | 116.09 | 116.09 | 116.09 | 116.09 | 116.09 | 116.09 |
| C4-C5-C6 | 121.36 | 121.36 | 121.36 | 121.36 | 121.36 | 121.36 | 121.36 |
| C4-C9-C8 | 117.49 | 117.49 | 117.49 | 117.49 | 117.49 | 117.49 | 117.49 |
| C5-C6-C7 | 117.82 | 117.82 | 117.82 | 117.82 | 117.82 | 117.82 | 117.82 |
| C6-C7-X19 | 121.48 | 121.48 | 124.84 | 119.04 | 119.60 | 119.64 | 119.14 |
| C7-C19/O19/H’19/H” | – | 111.30/ | 110.99/ | 111.43 | 118.39 | – | – | 117.68/117.63 |
| C7-C8-C9 | 121.33 | 121.33 | 121.33 | 121.33 | 121.33 | 121.33 | 121.33 |
| C1-C10-C11 | 124.46 | 124.46 | 124.46 | 124.46 | 124.46 | 124.46 | 124.46 |
| C11-C12-C13 | 120.15 | 120.15 | 120.15 | 120.15 | 120.15 | 120.15 | 120.15 |
| C12-C15-O17 | 115.89 | 115.89 | 115.89 | 115.89 | 115.89 | 115.89 | 115.89 |
| C13-O17-C18 | 118.67 | 118.67 | 118.67 | 118.67 | 118.67 | 118.67 | 118.67 |
| C13-C14-C15 | 119.52 | 119.52 | 119.52 | 119.52 | 119.52 | 119.52 | 119.52 |
| C14-C15-C10 | 121.78 | 121.78 | 121.78 | 121.78 | 121.78 | 121.78 | 121.78 |
| C15-C10-C1 | 117.78 | 117.78 | 117.78 | 117.78 | 117.78 | 117.78 | 117.78 |
| C10-C1-O16 | 119.95 | 119.95 | 119.95 | 119.95 | 119.95 | 119.95 | 119.95 |
| N19-O20-O21 | – | – | – | – | – | – | 124.69 |
| **Torsional angles** | | | | | | | |
| O16-C1-C2-H2 | 179.9 | 179.9 | 179.9 | –180.0 | –180.0 | –180.0 | 179.9 |
| H3-C3-C2-H2 | –180.0 | –180.0 | –180.0 | 180.0 | 186.0 | 180.0 | 179.9 |
| H3-C3-C4-C9 | 180.0 | 180.0 | 179.9 | 180.0 | –180.0 | 180.0 | 179.9 |
| O16-C1-C10-C11 | 179.9 | –179.9 | 179.7 | 180.0 | 180.0 | 179.9 | 179.9 |
| O16-C1-C10-C15 | 0.0 | 0.0 | –0.3 | 0.0 | 0.0 | 0.0 | –0.0 |
| C1-C10-C11-H11 | 0.0 | 0.0 | –0.0 | 0.0 | 0.0 | 0.0 | –0.0 |
| C12-C13-O17-C18 | 179.9 | 179.9 | 0.0 | 179.9 | 179.9 | 179.9 | 0.0 |
| C14-C13-O17-C18 | 0.0 | 0.0 | –179.9 | –0.0 | 0.0 | 0.0 | –179.9 |
3.5.2. Natural bond orbital analysis.

Natural bond orbital (NBO) of chalcones 1–7 and the important second-order perturbative estimates of donor-acceptor interactions values are displayed in Table 5. The occupancies and the energies of orbitals involved in primary delocalization are also reported. The interaction between filled and empty Non-bonding orbitals described for the hyper conjugative electron transfer process from the donor (filled) to the acceptor (vacant) orbital and the energy lowering due to this interaction is expressed as E2 [48]. The π-bonded electrons of C11–C12, C1–O16, and C14–C15 bonds in compound 5 delocalized onto non-bonding p-orbitals (vicinal) available on C10 and C13 carbon atoms are found to be very high (≈60, 72 and 57 kcal mol⁻¹) and this is primary delocalization of chalcone 3 non-bonding orbital of C1–C10 and C1–C2 bonds delocalization in antibonding orbitals of C2–C3 bond is around 236 and 86 kcal mol⁻¹. The chalcone, 3 methoxy oxygen, donates the electron from aromatic ring to α,β-unsaturated carbon atoms, the energies are enhanced to C1–C2 atoms. Chalcone 7 lone pair of electrons available on oxygen O20 and O21 is delocalized on to the antibonding orbital of N19–O20/O21 bond their delocalization energies are around ≈150 kcal mol⁻¹.

| Geometric parameters                  | 1        | 2        | 3        | 4        | 5        | 6        | 7        |
|---------------------------------------|----------|----------|----------|----------|----------|----------|----------|
| C13–O17–C18–H1′/H1″                 | –130.0   | 61.20/   | 179.9/   | 61.2/    | 179.9/   | 61.3/    | –179.9/  |
|                                       | –       | 179.9/   | –        | –        | –        | –        | –        |
| C5–C6–C7–X19                         | 179.9    | –        | 179.9    | –        | –        | –        | –        |
| C6–C7–C19–C20/O20                   | –        | –        | –0.0     | –        | –        | –        | –        |
| C14–C10–C1–C2                      | 0.0      | 0.0      | –0.4     | –0.0     | –0.0     | 0.0      | –0.0     |

X = F, Cl, Br, NO₂.

Table 5. NBO analysis of 1–7.

| Donor NBO          | Acceptor NBO | 1     | 2     | 3     | 4     | 5     | 6     | 7     |
|-------------------|--------------|-------|-------|-------|-------|-------|-------|-------|
| BD(C2)C–C3        | BD(C)C1–O16  | 19.23 | 19.20 | 20.96 | 19.80 | 19.76 | 20.30 | 18.54 |
| BD(C2)C–C3        | BD(C)C9–C8   | 12.03 | 12.41 | 12.71 | 12.06 | 12.10 | 11.68 | 13.03 |
| BD(C2)C–C9        | BD(C)C2–C3   | 16.21 | 16.25 | 16.37 | 16.52 | 16.45 | 16.60 | 14.99 |
| BD(C)C–C9         | BD(C)C4–C5   | 19.81 | 19.31 | 19.18 | 19.83 | 19.69 | 11.15 | 17.48 |
| BD(C)C–C9         | BD(C)C6–C7   | 22.11 | 22.00 | 22.51 | 22.36 | 22.31 | 19.51 | 23.51 |
| BD(C)C–C9         | BD(C)C2–C3   | 17.80 | 18.05 | 18.31 | 18.30 | 18.51 | 17.05 | 20.55 |
| BD(C)C–C9         | BD(C)C6–C7   | 18.81 | 18.51 | 18.59 | 20.93 | 20.61 | 22.76 | 19.44 |
| BD(C)C–C7         | BD(C)C9–C8   | 18.95 | 19.31 | 19.56 | 18.78 | 18.65 | 21.31 | 17.79 |
| BD(C)C–C7         | BD(C)C4–C5   | 17.61 | 17.75 | 17.51 | 17.87 | 18.50 | 17.79 | 21.43 |
| BD(C)C–C7         | BD(C)C1–O18  | 20.07 | 20.17 | 20.36 | 20.49 | 20.52 | 20.83 | 20.99 |
| BD(C)C–C7         | BD(C)C11–C12 | 22.46 | 22.50 | 22.27 | 22.39 | 22.71 | 23.10 | 22.95 |
| BD(C)C–C7         | BD(C)C13–C14 | 17.46 | 17.74 | 17.86 | 17.52 | 17.48 | 17.56 | 17.39 |
| BD(C)C–C7         | BD(C)C10–C15 | 15.21 | 15.35 | 15.43 | 15.61 | 15.66 | 15.52 | 15.49 |
| BD(C)C–C7         | BD(C)C13–C14 | 22.11 | 22.31 | 22.61 | 22.81 | 22.15 | 22.36 | 22.39 |
3.5.3. Atoms-in-molecules analysis.

Atoms-in-molecules (AIM) electron density topological analysis carried out for chalcone 1–7. Around 30 bond critical points (BCPs) with a (3,−1) topology between the atoms connected by a covalent bond (Table 6). The observed negative values for the Laplacian are indicated to the interaction of covalent or polarized bonds and are characterized by large $\rho_p$ values. Besides these one bonds, critical points are observed between the atoms C1 and O16 (carbonyl group) atom. The values of $\rho_{BCP}$ at the BCP are found to be 4.23 and $V^2 \rho_{BCP}$. Values are found to be 2.90. The positive magnitude of $V^2 \rho_{BCP}$ indicates the highly ionic nature of the carbonyl group in chalcones 1–7. In other bonds, is ionic nature of the carbonyl (C1–O16) group is confirmed by the positive Laplacian density at the critical bond point and high $\rho_{BCP}$ values [47,48]. In chalcones 4–7, another (1-3) BCP was also located between C7–X19 atoms. The Laplacian of the density at the BCP is attained positive and $V^2 \rho$ highly positive indicating the ionic nature of the C7–X19 bonds also.

3.5.4. Energies, dipole moments and polarizabilities.

HOMO-LUMO and dipole moment values for the chalcones 1–7 are listed in Table 7. HOMO-LUMO figures are displayed in Fig. 8. In the HOMO and LUMO orbitals, the introduction of electron-withdrawing groups for nitro, bromo, chloro, fluoro in para substitution for aromatic ring decreases the energies, and electron releasing methyl substituent and parent chalcone increases the energies of both HOMO and LUMO orbitals. Especially, compound 7 had the smallest HOMO-LUMO gap (ΔE = 0.127 eV), which signifies rapid electron and radical transfer between HOMO and LUMO orbital [49]. This could be one of the reasons that compound 7 showed good free radical scavenging activity. This finding reveals a close relationship to the electron density of compound 7 based on the resonance effect. The dipole moment is increased due to the presence of electron electron-withdrawing substituents (nitro, bromo, chloro, and fluoro) in the para position of the phenyl ring C=C– and decrease due to the presence of electron releasing methyl substituent. The order of dipole moments is 1 > 2 > 4 > 5 > 6 > 3 > 7.
### Table 6. AIM parameters for 1–7.

| Bond | $\rho \times 10^2$ | $\nabla^2 \rho \times 10^4$ | $\epsilon \times 10^4$ |
|------|--------------------|-----------------|-----------------|
| C1–O6 | 4.23 | 4.23 | 4.23 | 4.23 | 4.23 | 4.23 | 2.90 | 2.91 | 2.93 | 2.94 | 2.94 | 2.94 | 0.60 | 0.59 | 0.59 | 0.59 | 0.59 | 0.59 | 0.60 |
| C1–C2 | 3.50 | 3.49 | 3.49 | 3.49 | 3.49 | 3.50 | -8.49 | -8.45 | -8.45 | 8.46 | -8.46 | -8.46 | -8.47 | 1.08 | 1.08 | 1.08 | 1.09 | 1.09 | 1.09 | 1.07 |
| C2–C3 | 3.39 | 3.38 | 3.38 | 3.37 | 3.37 | 3.37 | -7.41 | -7.39 | -7.39 | -7.37 | -7.37 | -7.38 | -7.40 | 1.02 | 1.02 | 1.02 | 1.02 | 1.02 | 1.02 | 1.01 |
| C3–C4 | 3.03 | 3.03 | 3.03 | 3.04 | 3.04 | 3.05 | -9.71 | -9.72 | -9.72 | -9.74 | -9.74 | -9.74 | -9.89 | 0.80 | 0.80 | 0.80 | 0.81 | 0.82 | 0.82 | 0.87 |
| C4–C5 | 3.14 | 3.14 | 3.14 | 3.15 | 3.15 | 3.13 | -8.67 | -8.71 | -8.71 | -8.62 | -8.62 | -8.62 | -8.67 | 2.18 | 2.21 | 2.23 | 2.23 | 2.23 | 2.23 | 2.10 |
| C5–C6 | 3.13 | 3.14 | 3.12 | 3.13 | 3.13 | 3.15 | -8.59 | -8.59 | -8.50 | -8.53 | -8.53 | -8.53 | -8.65 | 2.11 | 2.14 | 2.14 | 2.20 | 2.20 | 2.20 | 2.08 |
| C6–C7 | 3.13 | 3.11 | 3.20 | 3.21 | 3.22 | 3.15 | -8.54 | -8.40 | -8.40 | -9.10 | -9.10 | -9.11 | -8.73 | 2.11 | 2.15 | 2.15 | 2.68 | 2.68 | 2.68 | 2.18 |
| C7–X19 | 2.55 | 2.52 | 2.56 | 2.57 | 2.57 | 2.64 | -0.60 | -0.60 | -1.41 | 1.40 | 1.41 | 1.41 | 7.48 | 0.31 | 0.31 | 0.71 | 0.71 | 0.72 | 1.17 |
| C7–C8 | 3.17 | 3.16 | 3.16 | 3.16 | 3.16 | 3.16 | -8.83 | -8.83 | -8.81 | -8.82 | -8.82 | -8.80 | 2.17 | 2.16 | 2.16 | 2.16 | 2.16 | 2.16 | 2.13 |
| C8–C9 | 3.09 | 3.09 | 3.09 | 3.09 | 3.09 | 3.08 | -8.43 | -8.43 | -8.42 | -8.41 | -8.41 | -8.40 | 2.37 | 2.39 | 2.39 | 2.37 | 2.37 | 2.36 | 2.32 |
| C9–C10 | 2.72 | 2.71 | 2.71 | 2.71 | 2.71 | 2.70 | -0.61 | -0.67 | -0.67 | -0.67 | -0.67 | -0.67 | -0.75 | 1.09 | 1.07 | 1.07 | 1.06 | 1.06 | 1.05 | 1.05 |
| C11–C12 | 3.08 | 3.08 | 3.08 | 3.07 | 3.07 | 3.07 | 3.06 | -0.83 | -0.83 | -0.81 | -0.80 | -0.80 | -0.80 | -0.81 | 1.91 | 1.92 | 1.92 | 1.95 | 1.90 | 1.90 | 1.90 |
| C12–C13 | 3.06 | 3.06 | 3.06 | 3.05 | 3.05 | 3.04 | -0.80 | -0.80 | -0.80 | -0.80 | -0.80 | -0.80 | -0.80 | 1.89 | 1.89 | 1.89 | 1.89 | 1.89 | 1.90 | 1.91 |
| C13–O16 | 3.07 | 2.88 | 2.88 | 2.88 | 2.88 | 2.90 | -2.89 | -2.88 | -2.88 | -2.87 | -2.87 | -2.87 | -2.83 | 1.00 | 0.09 | 0.09 | 0.10 | 0.10 | 0.10 | 0.13 |
| C16–C17 | 2.31 | 2.32 | 2.32 | 2.31 | 2.31 | 2.30 | -3.58 | -3.58 | -3.60 | -3.59 | -3.59 | -3.59 | -3.54 | 0.26 | 0.27 | 0.27 | 0.30 | 0.30 | 0.30 | 0.27 |
| C14–C15 | 3.15 | 3.14 | 3.15 | 3.15 | 3.15 | 3.16 | -8.58 | -8.56 | -8.56 | -8.57 | -8.57 | -8.57 | -8.62 | 2.23 | 2.24 | 2.24 | 2.24 | 2.24 | 2.24 | 2.25 |
| C15–C16 | 3.10 | 3.10 | 3.10 | 3.12 | 3.12 | 3.12 | -8.40 | -8.40 | -8.40 | -8.41 | -8.41 | -8.41 | -8.45 | 1.89 | 1.89 | 1.89 | 1.89 | 1.89 | 1.89 | 1.90 |

### Ring parameters

| Ring | $\rho \times 10^2$ |
|------|-----------------|
| 1    | C4–C5–C6–C7–C8–C9 | 1.99 | 1.99 | 1.99 | 1.99 | 1.99 | 1.99 | 2.00 |
| 2    | C10–C11–C12–C13–C14–C5 | 2.02 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.04 |

X = F, Cl, Br, NO$_2$.

### Table 7. HOMO–LUMO energies (eV) and dipole moments $\mu(D)$ of 1–7.

| Compds. | HOMO | LUMO | $\Delta E$ | $\mu_c$ | $\mu_c$ | $\mu_c$ | $\mu_{tot}$ |
|--------|------|------|------------|----------|----------|----------|------------|
| 1      | -0.253 | -0.095 | 0.158 | 1.909 | 2.964 | 0.201 | 5.351 |
| 2      | -0.245 | -0.090 | 0.155 | 0.077 | -2.508 | 0.017 | 2.510 |
| 3      | -0.210 | -0.065 | 0.146 | 0.278 | -3.849 | 0.005 | 3.859 |
| 4      | -0.233 | -0.084 | 0.149 | 2.125 | -1.628 | 0.000 | 2.677 |
| 5      | -0.240 | -0.093 | 0.147 | 2.688 | -1.666 | 0.000 | 3.163 |
| 6      | -0.239 | -0.093 | 0.146 | 1.517 | -0.746 | 0.000 | 1.691 |
| 7      | -0.236 | -0.106 | 0.130 | -6.909 | -0.547 | 0.000 | 6.931 |
Figure 8. HOMO-LUMO pictures of 1–7.

HOMO and LUMO orbitals are derived from pz orbitals of carbon, nitrogen, oxygen, and halogen (X= F, Cl, Br, and NO₂) atoms except pz orbitals of methoxy oxygen O–17 in 1–7. Compound 7, the pz orbital of α,β-unsaturated carbon C–4 linked with nitro substituted benzene ring does not participate to HOMO orbital, the same way pz orbital of LUMO orbital of a carbonyl group linked methoxy benzene ring also not involved LUMO orbital. In 2, 4, 5, and 6, all the pz orbitals are contributed to HOMO orbital else to C–1 atom, and the LUMO pz orbital of C–6, C–10, C–12, C–14, and O–17 orbital do not participate to LUMO orbital. The methoxy substituted chalcone 3, C–15, C–12, O–17, and C–18 atoms are not sharing pz orbital of HOMO. The LUMO orbitals of C–12, C–14, C–6, C–18, O–17, C–18, O–19, and C–20 are not involved in the LUMO orbitals.

The polarizability (α₀) and first-order hyperpolarizability (βtot) are related directly to the non-linear optical efficiency of structures. The calculated values of α₀, βtot by the finite field approach are given in Table 8. The calculated values of αij, βijk are converted into electrostatic units from atomic units (α: 1 a.u = 0.1482×10⁻²⁴ esu; β: 1 a.u = 8.6393×10⁻³³ esu). The electron-withdrawing substituent of NO₂, Cl, and F moieties of chalcones are increased the βtot values. The NLO character increasing according to the following order: 7 > 5 > 4 > 1 > 3 > 2 > 6.

|   | 1     | 2     | 3     | 4     | 5     | 6     | 7     |
|---|-------|-------|-------|-------|-------|-------|-------|
| αxx| 380.601| 769.0903| 74.3582| 89.8280| 95.0822| 95.9070| 140.5985|
| αyx| -0.028| 4.2553| 18.4817| 2.9736| 3.8946| 5.6540| 26.9686|
| αyy| 66.887| -114.3261| -113.1848| -111.3271| -91.2618| -125.0768| 10.0652|
| αxz| -91.575| -0.1728| -0.0154| -0.0044| 0.0000| 0.0001| -0.0035|
| αyz| -0.001| -0.0379| -0.0181| 0.0022| 0.0000| 0.0000| -0.0014|
| βxx| 138.5985| 138.5985| 138.5985| 138.5985| 138.5985| 138.5985| 138.5985|
| βyx| 26.9686| 26.9686| 26.9686| 26.9686| 26.9686| 26.9686| 26.9686|
| βyy| 10.0652| 10.0652| 10.0652| 10.0652| 10.0652| 10.0652| 10.0652|

Table 8. Polarizabilities and hyperpolarizabilities for 1–7.
3.5.5. Molecular electrostatic potential surfaces.

The MEP surface has been plotted for chalcones, and the representative diagram is given in Fig. 9. The red color region has appeared electronegative oxygen O\(^{-1}\) and O\(^{-17}\) in chalcones 1–7. The red-colored locations are polarized for the electrophilic attack \[49\], while the blue indicates a greater positive region and the maximum green color in the MEP surfaces regarding a potential halfway between the two extremes [red and blue] regions in chalcones 1–7.

![Figure 9. MEP diagrams of 3 and 7.](image)

3.6. Spectral properties.

The computational \(^1\)H and \(^{13}\)C NMR chemical shifts values are compared. Normally theoretical \(^1\)H chemical shifts values are higher when compared to experimental values, and some proton values have largely deviated from experimental values. The optimized structure, proton positions are three-dimensionally calculated in computation in \(^1\)H chemical shifts. The \(^{13}\)C chemical shifts are closer to the theoretical values. The correlation between experimental and theoretical \(^{13}\)C chemical shifts is shown in Fig. 10.

3.7. Charges.

Charges derived from NBO calculations are listed in Table 9, along with the Mulliken charges. From Table 9, it is inferred that all hydrogen and \(sp^2\) carbons of some of the carbon atoms attain positive charges (C–3, C–6, C–9, C–10, C–14, and C–18) while the remaining
carbon atoms attain negative charges. The charge sharing the molecule is a significant influence of the atoms possess negative and positive.

![Graphs showing correlation between experimental and theoretical $^{13}$C chemical shifts for 1–7.](https://doi.org/10.33263/BRIAC126.71597176)

**Figure 10.** Correlation between the experimental and theoretical $^{13}$C chemical shifts for 1–7.

It is observed that the negative charge on O17 and O19, resulting in polarizing the positive charge on the adjacent atoms of C–3, C–6, C–9, C–10, C–14, and C–18. In this, positive carbon atoms act as an electrophilic center in the molecule. The remaining carbon atoms are acting nucleophilic center the atoms. The charges predicted from NBO calculations are slightly higher than those of Mulliken charges on all carbons except those on C–3, C–6, C–9, C–10, C–14, and C–18.

### 3.8. Antimicrobial studies.

The antimicrobial activity of chalcones 1–7 was studied difference concentration of the disc diffusion method using the Kirby-Bauer method [50]. The bacterial strains viz., *Staphylococcus aureus*, *Escherichia coli*, and fungal strains viz., *Candida albicans*, *Aspergillus flavus* were used for this study. The zone of inhibition (mm) of chalcones 1–7 is tested for both bacterial and fungal strains and values [51,52] listed in Table 10. The selected photographs are displayed in Fig.11. The Ethanol solvent was used to control the Gentamicin and Fluconazole standards for bacterial and fungal strains, respectively. The compounds 2, 5, and 6 demonstrated higher activity against antibacterial strains *E. coli* and *S. aureus*. 

https://biointerfaceresearch.com/
Table 9. Charges (Mulliken and Natural) of 1–7.

| Atoms | MC   | NC   |
|-------|------|------|
| C–1   | –0.6327 | 0.5797 |
|      | –0.6471 | 0.5182 |
| C–2   | –0.1133 | –0.2934 |
|      | –0.2851 | –0.0596 |
| C–3   | 0.2674  | –0.0836 |
|      | 0.2741  | –0.0852 |
| C–4   | –0.4531 | –0.1554 |
|      | –0.4623 | –0.1594 |
| C–5   | –0.2296 | –0.1999 |
|      | –0.2305 | –0.1983 |
| C–6   | 0.5787  | –0.3147 |
|      | 0.5898  | –0.0128 |
| N–7   | –0.4323 | –0.2131 |
|      | –0.5836 | –0.2037 |
| N–8   | –0.2137 | –0.1516 |
|      | –0.2331 | –0.1546 |
| C–9   | 0.8313  | –0.1176 |
|      | 0.9418  | –0.1065 |
| C–10  | 1.3934  | –0.1462 |
|      | 1.5012  | –0.1575 |
| C–11  | –0.7931 | –0.1567 |
|      | –0.8664 | –0.1597 |
| C–12  | –0.4000 | –0.2431 |
|      | –0.4027 | –0.2444 |
| C–13  | –0.5321 | –0.5416 |
|      | –0.5417 | –0.3465 |
| C–14  | 0.3361  | –0.2931 |
|      | 0.3394  | –0.2901 |
| C–15  | 0.6931  | –0.1326 |
|      | 0.7081  | –0.1344 |
| O–16  | –0.2416 | 0.5914  |
|      | –0.2486 | –0.5903 |
| O–17  | –1.5070 | 0.5344  |
|      | –1.5200 | –0.5351 |
| O–18  | 0.1831  | –0.5317 |
|      | 0.1811  | –0.2061 |
| X–19  | –        | –0.0699 |
|      | –0.5913 | –0.1527 |
| O–20  | –        | –        |
| C–20  | –        | –        |
| O–21  | –        | –        |

X = F, Cl, Br, NO₃; MC – Mulliken charges; NC – Natural charges.

Table 10. Antibacterial and antifungal activities of 1–7.

| Compds. | Staphylococcus aureus | Escherichia coli | Candida albicans | Aspergillus flavus |
|---------|----------------------|-----------------|------------------|-------------------|
|         | G (18 mm)            | G (18 mm)       | F (15 mm)        | F (16 mm)         |
|         | µg/mL                | µg/mL           | µg/mL            | µg/mL            |
|         | 10 | 20 | 40 | 10 | 20 | 40 | 10 | 20 | 40 | 10 | 20 | 40 | 10 | 20 | 40 | 10 | 20 | 40 |
| 1      | 13 | 15 | 22 | 6 | 10 | 12 | 11 | 22 | 11 | 15 | 12 | 14 | 12 | 18 | 20 | 16 | 14 | 18 | 20 | 16 |
| 2      | 14 | 17 | 24 | 8 | 15 | 17 | 14 | 19 | 18 | 13 | 14 | 14 | 14 | 18 | 22 | 17 | 14 | 20 | 22 | 17 |
| 3      | 18 | 9  | 14 | 7 | 10 | 11 | 12 | 19 | 10 | 14 | 12 | 12 | 11 | 14 | 20 | 17 | 13 | 14 | 15 | 17 |
| 4      | 16 | 20 | 16 | – | 18 | 18 | 17 | 18 | 9  | 13 | 14 | – | 13 | 15 | 16 |          |          |          |          |
| 5      | 16 | 16 | 18 | – | 13 | 18 | 17 | 18 | 9  | 13 | 14 | 15 | – | 13 | 15 |           |          |          |          |
| 6      | 9  | 7  | –  | 12 | 7  | 9  | 30 | 20 | 18 | 18 | 20 | 7  | 11 | – | 18 |          |          |          |          |

*Activity for the reference compound: for bacteria (1–7) G – Gentamicin was used as reference; for fungus (1–7) F – Fluconazole was used as reference.
The remaining substituted chalcones were satisfactory activity for the strain. Antifungal activity data (Table 8) if could be observed that all the chalcones 1–7 are a good activity for strain *Candida albicans* and moderate activity for *Aspergillus flavus* strains.

### 4. Conclusions

The known substituted chalcones 1–7 were characterized by using experimental and computational methods. The molecular properties such as bond length and bond angles were theoretically investigated by the optimized structure, and favored conformation of chalcone 3 was investigated. The nature and origin of the intramolecular electrons transition of HOMO-LUMO optimized structure were derived from all the synthesized compounds. The electrophilic and nucleophilic reactive sites probable binding sites of the compounds were obtained by using MEP surface analysis. The polarizability and hyperpolarizability values were calculated, and NLO activity was determined by the substituted chalcones 1–7. The Mulliken charges, NBO, natural charges, $^1$H, and $^{13}$C NMR values were also compared experimentally and theoretically. The antibacterial and antifungal activity was derived by the disc diffusion method. All the substituted chalcones were good active against corresponding strains.

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Conflicts of Interest

The authors declare no conflict of interest.

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