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Synthesis of Two Chalcones Compounds, Theoretical Investigation and Biological Activity Study

Zainab Y. Kadhim[1*], Wafaa Mahdi Alkoofee[2], Ameena N. Seewan[3], Asstabraq Mohsin Yasir[4]

[1]College of Veterinary Medicine, Al-Muthanna University, Al-Muthanna, Iraq
[2,4]Department of Chemistry, College of Science, Al-Muthanna University, Al-Muthanna, Iraq
[3]Department of Science, College of Basic Education, Al-Muthanna University, Al-Muthanna, Iraq

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***Corresponding author:** Zainab Y. Kadhim
College of Veterinary Medicine, Al-Muthanna University, Al-Muthanna, Iraq.

Abstract **Original Research Article**

The goal of this study was to synthesize two chalcone compounds and describe them as antibacterial compounds. These compounds are synthesized using a microwave. The element C.H.N analyzer, IR (Infrared Radiation) spectra, and UV (Ultraviolet-Visible) spectra were used to characterize the newly synthesized chalcones. A semi-empirical method (PM3) was used to evaluate the heat of formation ΔH°_{f}, binding energy ΔE_b, HOMO and LUMO for synthesized compounds, as well as the vibration frequencies and electronic transitions,. *Staphylococcus aureus* and *E. coli* were used as test organisms for the antibacterial activity of compounds (CH_1 and CH_2), and the results indicate a moderate to low activity and sensitivity against germs.

Keywords: Chalcones, Antibacterial activity, Theoretical study.

INTRODUCTION

For their potential to fight germs, chalcone derivatives are a class of substances that have undergone substantial research [1-11]. Chalcones have a unique chemical structure that consists of two aromatic rings connected by a three-carbon, -unsaturated carbonyl system. The antibacterial activity of chalcone derivatives has been documented in numerous experiments against a variety of bacteria, including strains [3-5] of both Gram-positive and Gram-negative bacteria. Chalcones are thought to have a variety of targets and modes of action that work together to fight germs. In order to combat drug-resistant types of bacteria, such as methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE), chalcone derivatives may be an option. Additionally, derivatives of the chalcone have proven to be antibacterial against a variety of bacteria, including strains [6–12] of both Gram-positive and Gram-negative bacteria. This wide range of activity is beneficial since it opens up the possibility of alternative applications for treating different bacterial illnesses. In comparison to traditional antibiotics, chalcone derivatives frequently have a distinct mode of action. They can target numerous bacterial parts or metabolic processes, making it challenging for bacteria to evolve resistance. An approach to combat antibiotic resistance is offered by this alternative mechanism of action. Chalcone derivatives have additionally demonstrated synergistic interactions with traditional antibiotics [12–16]. This implies that they can increase the efficacy of already-in-use antibiotics, perhaps overcoming bacterial resistance and enhancing therapeutic results [17–20]. Other. Chalcone compounds have shown anti-biofilm action, which prevents the formation of biofilm and makes bacteria more susceptible to antibiotics. It is important to note that although though chalcone derivatives have the potential to be effective antibacterial agents, further study is still required to completely comprehend their mechanisms of action, enhance their qualities, and assess their safety and efficacy in clinical settings [21–23].

Experimental:

2.1 Instrumentation

An open capillary is used to determine all melting points. Also, element C.H.N analyzer was carried out on an EM-017. These instruments (Mth) are based in the department of chemistry laboratory/Faculty of Science/AL-Muthanna University. The FT-IR spectra in the range (4000-400cm^{-1}) was recorded as KBr disc on IR-Prestige-21(single beam path laser)/Shimadzu Fourier transform infrared spectrophoto meter. UV-Visible spectra were measured using UV1800PC

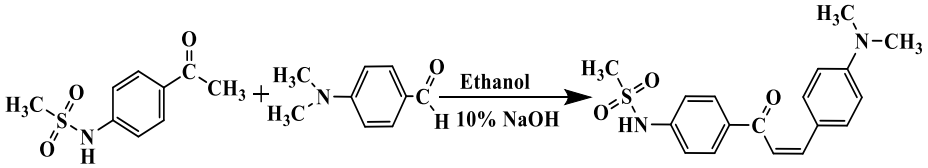
Shimadzu, UV-Visible Spectrophotometer in range-200 (800nm). All the chemicals supplied by BDH, Fluka and Sigma-Aldrich.

2.2 General Procedure for Preparation of Chalcones (CH_1-CH_2) [24]

The chalcones (CH_1 and CH_2) prepared by the reaction of the mixture of 0.01 mole of substituted acetanilide with 0.01 mole of substituted aldehyde and a catalytic quantity of Sodium hydroxide (10%) and a few drops of ethanol. The mixture was irradiated in microwave oven for 1min. and 300W, then cooled at room temperature. The reaction monitored by T.L.C. The product poured into a glass containing ice-water. Furthermore, the precipitate was collected by filtration. Finally, a suitable solvent used to recrystallize the products. The following methods were used for chalcones preparations:

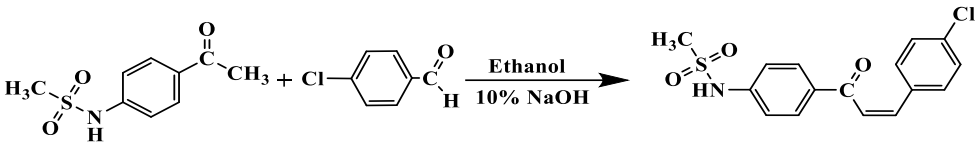
***N*-(4-(3-(4-(Dimethylamino) phenyl) acryloyl) phenyl) methanesulfonamide (CH_1)**

It was synthesized by reacting *N*-(4-acetylphenyl) methanesulfonamide (0.01 mole, 2.13gm) with 4-(dimethylamino) benzaldehyde (0.01mole, 1.49gm) in basic medium and using abs. ethanol as a solvent the mixture was irradiated in microwave oven for 1min. and 300W, then cooled at room temperature. Yield. 91%, m.p. 95-97^{0}C. IR ($\bar{\upsilon}$, cm^{-1}, KBr disk): 1645(C=O of α,β-unsaturated). Recrystallize with dimethyl ether.



***N*-(4-(3-(4-Chlorophenyl)acryloyl)phenyl)methanesulfonamide(CH_2)**

It was synthesized by reacting *N*-(4-acetylphenyl) methanesulfonamide (0.01mole, 2.13gm) with 4-chlorobenzaldehyde (0.01mole, 1.40gm). The mixture was irradiated in microwave oven for 1min. and 300W, then cooled at room temperature Yield. 78%, m.p. 84-86^{0}C. IR ($\bar{\upsilon}$, cm-1, KBr disk): 1644 (C=O of α,β-unsaturated). Recrystallize with methanol.



3. RESULT AND DISCUSSION

3.1 Characterization of chalcone compounds ($CH_1$and CH_2)

The analytical data for compounds including the calculating Values of C.H.N analysis, UV-Vis. and IR spectra revealed the following values for prepared compounds as follows:

***N*-(4-(3-(4-(Dimethylamino)phenyl)acryloyl)phenyl)methanesulfonamide(CH_1).**

λ_{max}= 329nm and R_f= 0.73. Elemental analysis ($C_{18}H_{20}N_2O_3S$); (M.Wt: 344.43). Calc. C, 62.77; H, 5.85; N, 8.13%. Found. C, 61.87; H, 5.97; N, 9.08. FT-IR [cm^{-1}]: *υ*(Conj. C=O) 1691.63*s*; *υ*(Conj. C=C) 1610.61*s*; *υ*(C=C stret.) 1562.39*s*, 1438*m*; *υ* (NH Stret.) 3327.32*b*; *υ*(NH Bend) 1656.91*s*; *υ*(O=S=O) 1170.83*m*; υ(C-N) 1371.43*s*.

***N*-(4-(3-(4-Chlorophenyl)acryloyl)phenyl)methanesulfonamide(CH_2).**

λ_{max}= 289 nm and R_f = 0.69. Elemental analysis ($C_{16}H_{14}ClNO_3S$); (M.Wt: 335.81). Calc. C, 57.23; H, 4.20; N,4.17%. Found. C, 57.57; H, 4.87; N, 3.99. FT-IR [cm^{-1}]: *υ* (Conj. C=O) 1705.07*s*; *υ*(Conj. C=C) 1654.92*s*; *υ*(C=C stret.) 1539.20*m*; *υ*(NH Stret.) 3232.70*b*; *υ*(O=S=O) 1172.72*s*; *υ*(C-Cl) 790.81*m*.

3.2 Theoretical Studies

The most significant molecular modeling program is (HyperChem8.0). It is possible to sketch molecules by choosing their internal coordinates and then estimating their spectral qualities using the molecular modeling programs contained in the quantum mechanics program called hyper chem. This program actually demonstrated a significant effort in the area of scientific research. It is an essentially empirical program that offered accurate answers to the problems encountered during the research of some hazardous compounds, highly sensitive materials, or materials with high levels of activity [25].

3.2.1 Energies:

One of the most useful notions in science is energy. The energetic analysis can forecast which molecular processes are likely to occur or are capable of occurring. Energy is used in all computational chemistry techniques such that the system with the lowest energy is the most stable [26]. As a result, a molecule's form corresponds to the structure with the lowest energy. In this work, the heat of formation ($\Delta H°_f$), binding energy

(ΔE_b), and frontier orbitals (HOMO & LUMO) for chalcone compounds were determined using the PM3 method. (Table 1), and the energy calculation demonstrated that the compound CH_1 was more stable than the compound CH_2.

Table 1: Energy by K.J.mol^{-1} unit, HOMO and LUMO energy

Comp.	ΔH°_f	ΔE_b	HOMO	LUMO	ΔE_{gab}
CH_1	-35814.26	-16296.52	-1.2533	-9.295	8.04
CH2	-185.0496	-55015.21	-0.1706	-7.930	7.76

3.2.2 Theoretical Vibration Frequencies of CH_1 and CH_2 compounds:

PM3 method was used to calculate the vibration frequencies of CH_1 and CH_2 compounds (Table 2). The theoretical spectra derived from semi-empirical calculations offer to explain the experimental spectrum peaks. The figure shows the assignment of chalcone compound using the most typical estimated vibrational frequencies. The theoretical wave number for the prepared chemical differs from the preceding values; however, these deviations are generally acceptable in computational chemistry.

Table 2: Experimental and theoretical vibrational frequencies of CH_1 and CH_2 compounds

Comp.	υ(NH)	υ(C=O)	υ(C=C)$_{Conj.}$	υ(C=C).	υ(C-Cl)	υ(O=S=O)
CH_1	3300.43* 3327.32** -0.8)***(	1670.55* 1691.63 ** (-1.24)***	1630.33* 1610.61 ** (1.22)***	1540.66* 1562.39 ** (-1.39)***	-----	1175.99* 1170.83 ** (0.44)***
CH_2	3370.40* 3232.70** (4.26)***	1700.01* 1705.07** (-0.29)***	1670.02* 1654.92** (0.91)***	1610.00* 1539.20** (4.60)***	800.02* 790.18** (1.25)**	1180.22* 1172.72** (0.63)***

Where:

*: Theoretical value

**: Experimental value

***: Error %

3.2.3-Theoretical Electronic Spectra:

The theoretical electronic spectra of CH_1 and CH_2 compounds were evaluated by PM3 method which showed that there is high acceptable between the experimental and theoretical data.

Table 3: λ_{max} of CH_1 and CH_2 compound

Comp.	λ_{max} Experimental (nm)	λ_{max} Theoretical (nm)
CH_1	**392**	**318**
CH_2	**289**	**303**

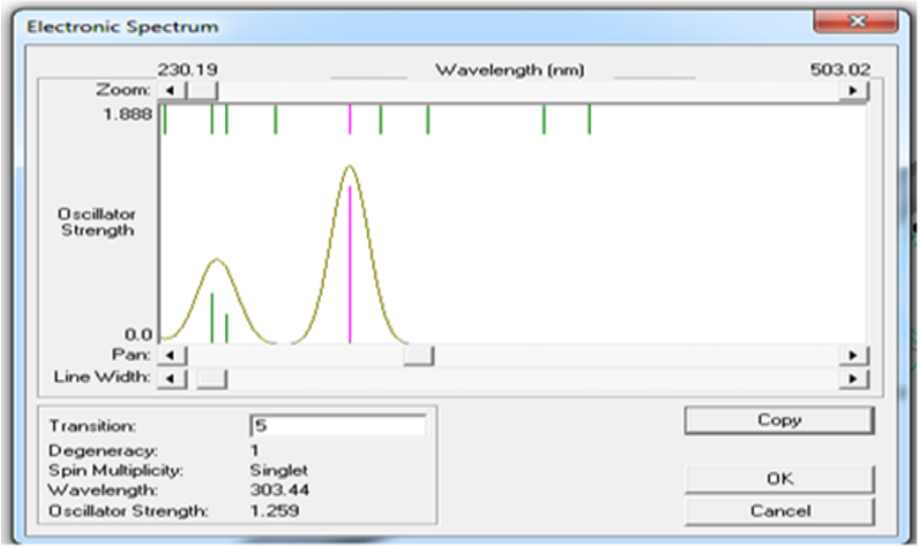


Figure 1: Electronic spectrum of CH_1 compound

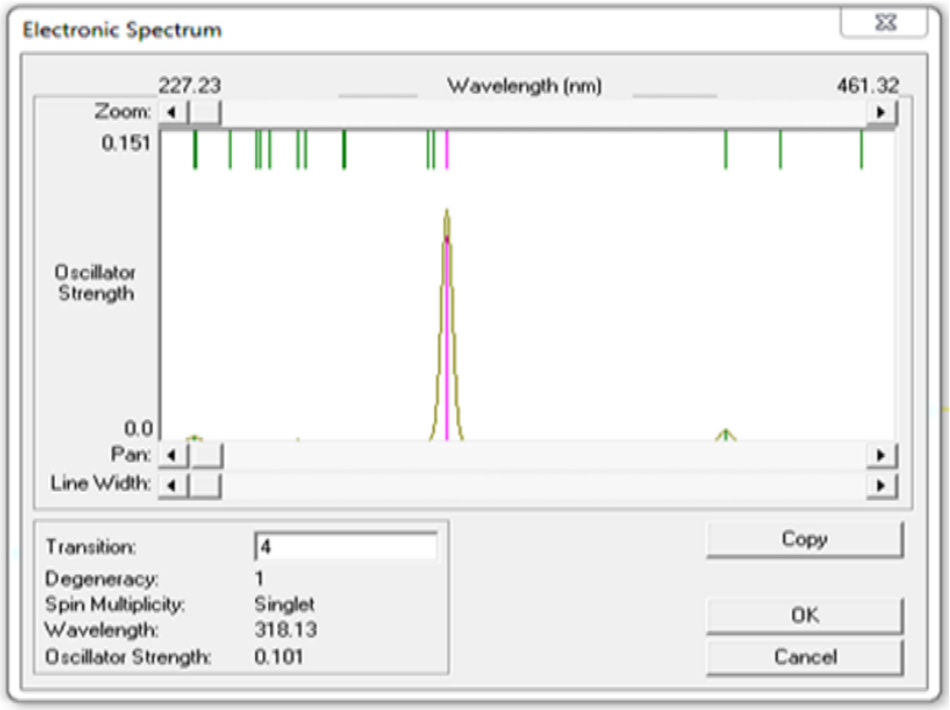


Figure 2: Electronic spectrum of CH_2 compound

4. Antimicrobial properties

The paper disk diffusion technique was used for investigating the antibacterial activity of CH_1 and CH_2 compounds against Staphylococcus aureus and E.coli. Three loops of each culture were transferred into test tubes containing 2 ml of nutrient broth and incubated for a 24-hour period at 37^0C. After incubation, each bacteria broth culture was mixed with saline to obtain turbidity that was visually equivalent to No.1 Mac Farland standard tube. Muller-Hinton agar was produced and poured into Petri plates, then swabbed with bacterial suspensions and left for 15 minutes before inserting sterile 6 mm diameter filter paper discs impregnated with (CH_1, and CH_2) concentrations of test compounds. Gentamicin disc (10g/disc) To ensure that common antibiotics were effective against the test bacterium, a disc was employed as a positive control. The sample discs and the standard antibiotic discs were carefully placed on the agar plates that had already been inoculated with the test bacteria, with DMSO serving as a negative control. The plates were then turned over and let to sit for 24 hours at 37^0C. Following incubation, the diameter of the millimeter-sized zones of inhibition was measured to determine the test compounds' antibacterial properties. While Staph. aureus has moderate activity and *E. coli* exhibits low inhibition zone diameter at concentrations of 0.001 g/ml, CH_1 compounds have no effect on *E. coli* at 0.01 g/ml.

In addition to the compounds' activity, these results may also be influenced by the compounds' concentration and the antimicrobial sensitivity test technique that was employed. Particularly sensitive to all prepared compounds was *Staphylococcus aureus.*

Table 4: The antimicrobial capacity of CH_1 and CH_2 compounds

Comp.	***Staphy.aureus***		***Ecoli***	
	1	**2**	**1**	**2**
	Concentrations			
CH_1	9mm	15mm	18mm	*
CH_2	8mm	13mm	12mm	12mm

Where:

1=0.001g/ml

2=0.01g/ml

*:No effect

Figure 3: The Zone of inhibition (mm) of $CH_1$and CH_2 against the selected bacterial strains

CONCLUSION

We describe the synthesis of two chalcone (CH_1 and CH_2) molecules in this paper. FT-IR, UV-Visible, and elemental analysis (C.H.N.) were used to characterize the products, which included CH_1 and CH_2 compounds. Homo & Lomo, or the heat of formation. Using the HyperChem8.0 program, electronic and vibration frequencies were computed. When tested against all the examined bacteria, the biological activity of the produced compounds demonstrated a range of biological activity. To assess the biological activity and toxicity of these chemicals and determine their efficacy and safety, more research is required.

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