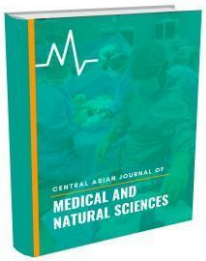

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Article

Synthesis, Charactarizit and Evaluation of Bacterial Efficacy and Study of Molecular Substrates of Cobalt (II) Complex [Co (2-(benzo[d]thiazol-2-yloxy) acetohydrazide) (H_2O) (Cl_2)]

Mahmoud Mehdi Saleh[1], Fahad Farhan Rokan[2], Jamil Nadhem Saleh[3] , Mohammed Jwher Saleh[4]

1. Tikrit University, College of Education for Pure Science, Departement of Chemistry
2. Kirkuk, Ministry of Education, Departement of Chemistry
3,4 Salah al-Din Education Directorate, Iraq

* Correspondence: jamelnadhemsaleh@gmail.com

Abstract: Due to the importance of medical and biological cobalt complexes, in this research, a new complex of cobalt complexes was prepared [Co (2-(benzo[d]thiazol-2-yloxy)acetohydrazide)(H_2O)(Cl_2)] using 2-(benzo[d]thiazol-2-yloxy)acetohydrazide as a basic alkand.the lycand was prepared from the reaction of the ester with aqueous hydrazine. , using physical techniques (color, melting point, R_f) and spectral methods (FT-IR infrared spectrum, carbon-Proton NMR spectrum ^{1}H-NMR , ^{13}C-NMR, SEM & XRD) the correctness of the compositions of the prepared compounds was confirmed , and then the bioeffectiveness of the series of compounds was studied on two types of Gram-positive and Gram-negative bacteria (***Staphylococcus aureus*** and ***Escherichia coli***), And the study of the molecular Docking of the complex and the ligand on Pseudomonas aeruginosa bacteria and the calculation of the binding energy and RMSD values.

Keywords: Hydrazide, Benzothiazole, Complexes, Molecular Docking, Biological Activity

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1. Introduction

Recently, fused heterocyclic compounds have piqued the interest of medicinal chemists due to their considerable contribution to the biological profile of medications, such as anticancer treatments [1, 2]. Researchers have paid close attention to benzothiazole alternatives because of their widespread usage in pharmaceutical and agricultural chemistry. As a result, the research of benzothiazole derivatives is very significant right now because of their crucial biological and biophysical features, such as antimicrobials [3, 4] and antifungal agents [5]. Several substituted benzothiazole compounds have been found as effective antihelmintic agents [6]. Amino benzothiazole compounds can exhibit a wide range of biological actions, including anti-Parkinson's (a nervous system disorder), dopamine antagonists, antimicrobial, and antihistamine properties [7].

Benzothiazole hydrazine is a bicyclic structure that belongs to the hydrazide group. Because of their multi-reaction chemical composition, benzothiazole derivatives have been extensively researched and are regarded as the nucleus structure for the synthesis of novel benzothiazole derivatives [8]. They have demonstrated a wide range of chemotherapeutic activities, including antimicrobials [9], anti-pain [10], antitumor agents [11], anti-inflammatory [12], anti-cancer [13], antibacterial [14], antifungal [15], anti-HIV [16], is a

potent animal growth stimulator [17]. Mineral complexes, in addition to a variety of benzothiazole derivatives, have antibacterial and antifungal properties [18]. Many drugs' activities have been shown to be increased when the chemical is regarded a ligand in combination with minerals [19].

Hydrazides are versatile compounds that can be used to create heterocyclic Xsystems. Furthermore, because of their diverse biological properties, such as antidiabetic [20], antimalarial [21], anticancer [22], antimicrobial [23], antioxidant [24], anti-inflammatory [25], and anxiolytic [26], hydrazide-hydrazones continue to be of great interest in the field of medicinal chemistry.

2. Materials and Methods

Material

Without any additional purification, all of the compounds utilized in this research investigation were acquired from BDH, Fluka, and Aldrich.

Devices Used:

Melting points were measured using a Thermoelectric Melter 9300 at a scale of 400-4000 cm-1, a Shimadzu FT-IR 8400S spectrophotometer, and a Bruker apparatus running at 400 MHz for 1H-NMR and 13C-NMR spectra, respectively. Fluka silica gel plates were used in thin-layer chromatography (TLC) and had a thickness of 0.2 mm. UV light was used to restore visibility after the plates had been activated with fluorescent silica gel. The scanning electron microscope (SEM) (Czech Republic/Belsorp Mini II/TE SCAN) was utilized.

Preparation of 2-(benzo[d]thiazol-2-yloxy)acetohydrazide (MH1) [27]

A solution of ethyl 2-(benzo[d]thiazol-2-yloxy) acetate (0.01 mol) and hydrazine hydrate 99% (0.2 mol) in abs ethanol (50 mL) was refluxed for three hours. Excess ethanol was eliminated through distillation. Upon cooling, 2-(benzo[d]thiazol-2-yloxy) acetohydrazide began to separate. It was filtered and recrystallized with ethanol, yielding an 84% product with a melting point of 190 degrees Celsius and a faint yellow color.

Preparation of Complex (MH2) [28]

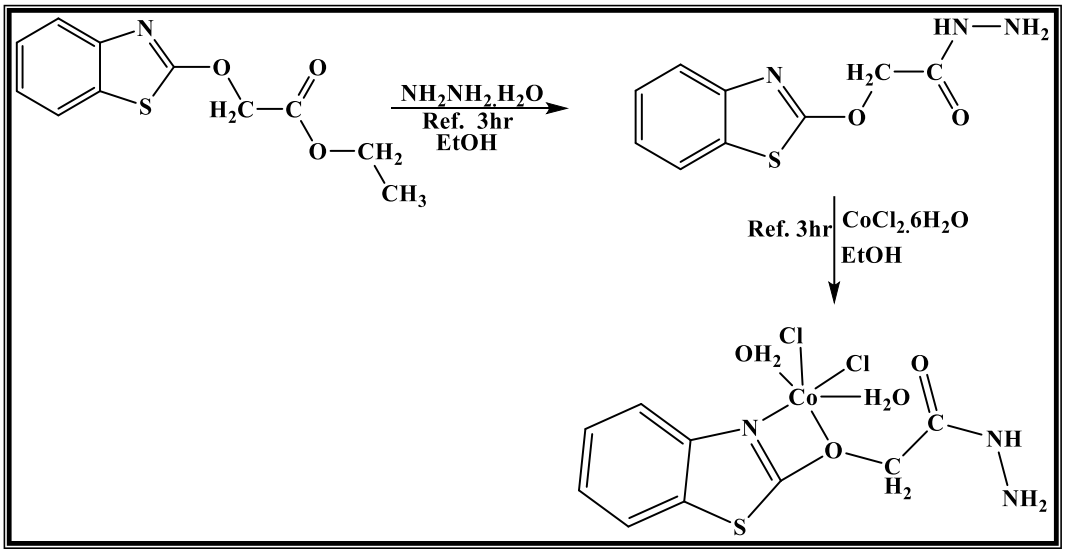
00.2 g dissolved from 2-(benzo[d]thiazol-2-yloxy)acetohydrazide in 10mL of absolute ethanol was mixed with 0.210 g of CoCl2. 6H2O dissolved in 10mL of distilled water and heated the mixture with a release at a temperature of 150C for three hours, then the solution was cooled, concentrated and recrystallized in the resulting had a pink color and a melting point of 300

Biological activity study:

Biological activity has been measured using the Kirby Bauer movement's propagation method, which entails spreading 0.1 ml of bacterial solution on Nutrient Broth plates and allowing them to absorb the fluid for five minutes [29, 30]. To make holes in each dish, a five mm cork and a cork plunger were utilized [31,32]. After that, 0.1 ml of the fourth hole's generated solutions-which used ciprofloxacin as a reference sample-were incubated for twenty-four hours at 37 °C. The inhibitory zone widths around each hole have been measured in millimeters using Prescott's method [33,34,35].

3. Results and Discussion

This study involved the preparation of several compounds, as the scheme(1) illustrates.



Scheme 1. Path of the Ready Combination (MH1, MH2)

Characterization of hydrazide [36]

FT-IR(KBr): (3224) ν(N-H), (2970) ν(C-H), (3083) ν(Ar-H), (1677) ν(C=O), (1604) ν(C=N), (3309,3390) ν(NH_2), (1475,1550) ν(C=C), as shown in the figure (1). 1H-NMR (DMSO-d_6) δ(PPm): (4.37) (s, NH_2), (9.47) (s, NH), (4.85) (s, CH_2), (7.18-7.68) (m, Ar-CH). as shown in figure (2). 13C-NMR (DMSO-d_6) δ(PPm) : (43.76) (CH_2), (165.84) (C=O), (169.56) (C=N), (111.85-137.75) (m, Ar-CH). as shown in figure (3).

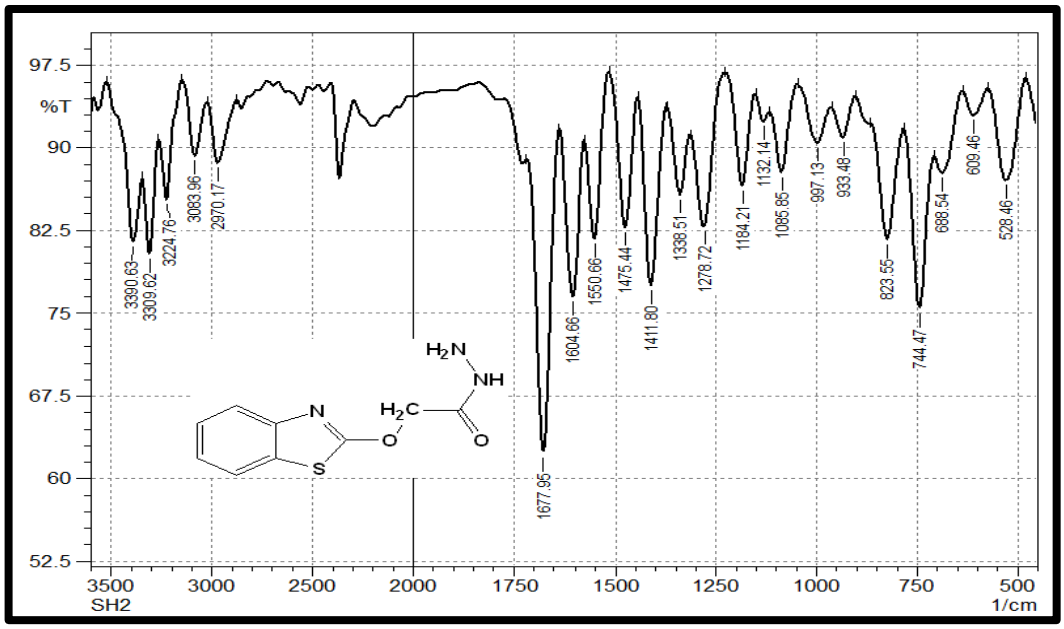


Figure. The Infrared Spectrum of the Compound (MH1)

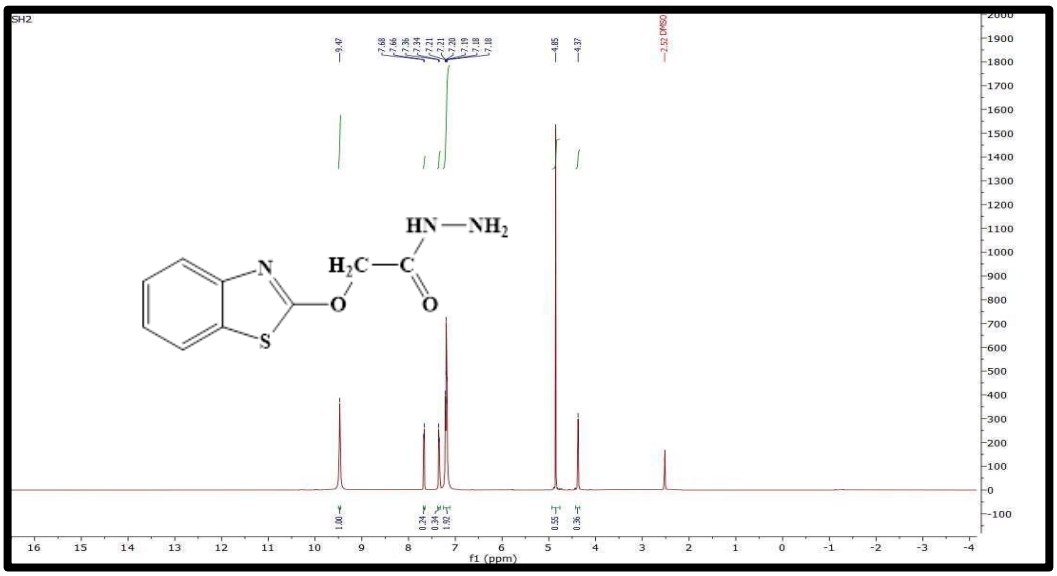


Figure 2. The 1H-NMR Spectrum of the Compound (MH1)

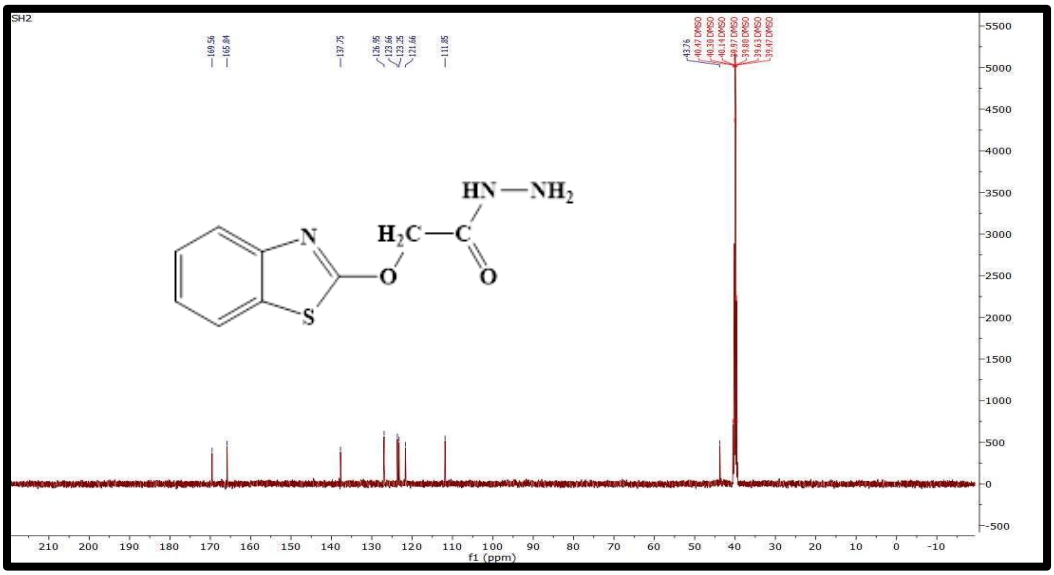


Figure 3. The 13C-NMR Spectrum of the Compound (MH1)

Characterization ofxComplex MH2 [37];

FT-IR(KBr): (3242) ν(N-H), (2904) ν(C-H), (3018) ν(Ar-H), (1652) ν(C=O), (1606) ν(C=N), (3315-3390) ν(NH_2), (1461,1564) ν(C=C), (1010) ν(C-N), (759) ν(N-N), (1276,1336) ν(C-O),as shown in the figure (4). 1H-NMR (DMSO-d_6) δ(PPm): (4.84) (s, NH_2), (10.26) (s, NH), (3.78) (s, CH_2), (7.11-7.55) (m, Ar-CH). as shown in figure (5). 13C-NMR (DMSO-d_6) δ(PPm): (60.37) (CH_2), (170.47) (C=O), (164.66) (C=N), (123.38-140.45) (m, Ar-CH). as shown in figure (6).

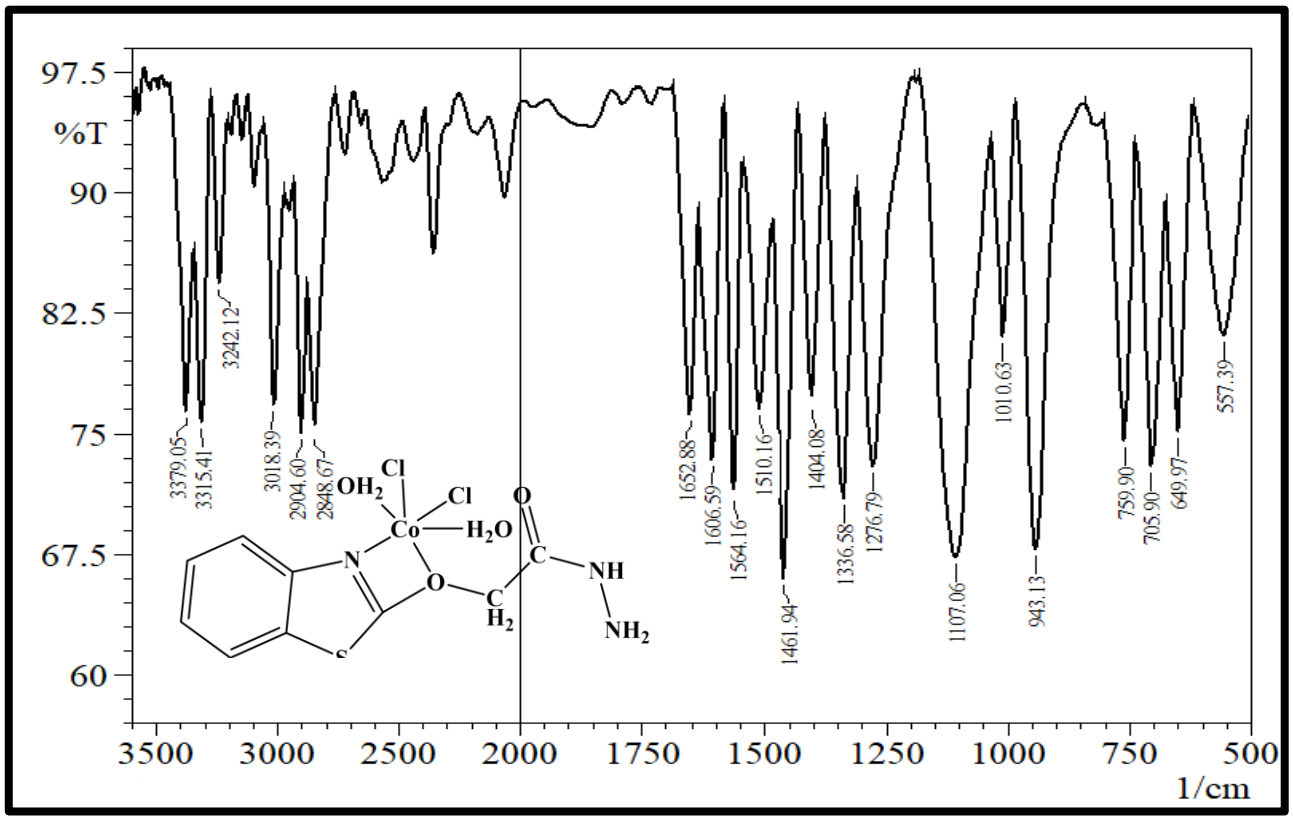


Figure (4): The infrared spectrum of the compound (MH2)

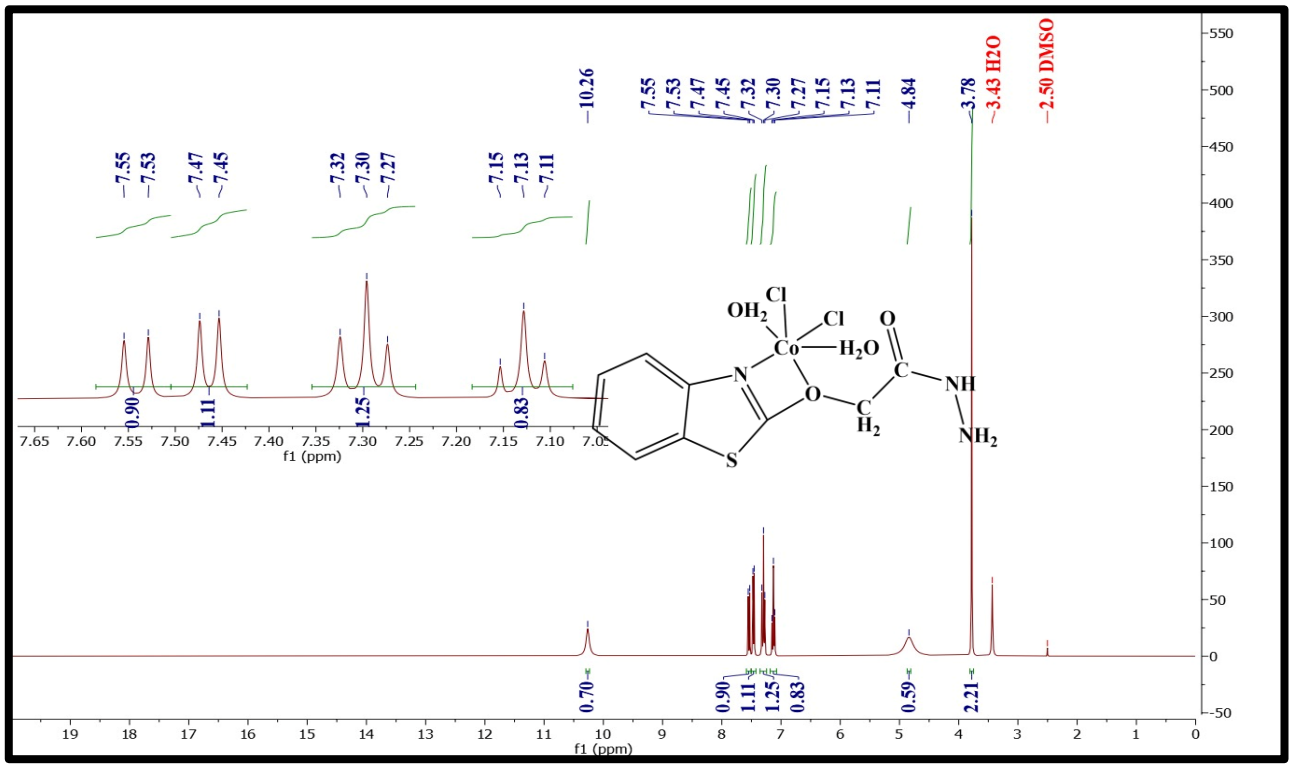


Figure (5): The 1H-NMR spectrum of the compound (MH2)

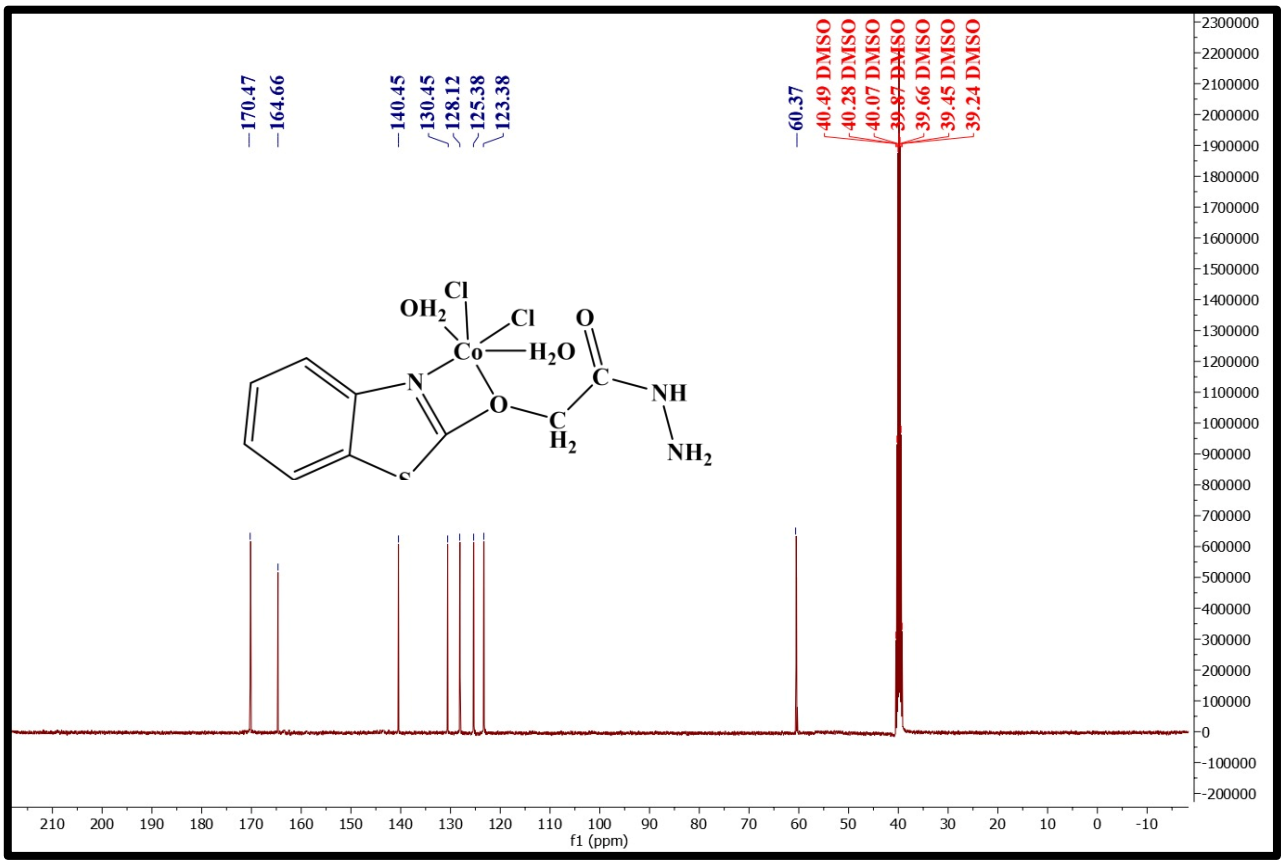


Figure (6): The 13C-NMR spectrum of the compound (MH2)

The Results of SEM:

Scanning electron microscope (SEM) technology is based on the use of a high-energy focused electron beam, which in turn interacts with the surface of the sample exposed to it, resulting in obtaining topographic images, as well as generating a different set of signals on the surface of the solid sample under test, and this technique can provide a lot of information about the sample surface, and this technique depends mainly on the area of the spot that is exposed to the electronic beam as well as the extent of its impact on it, where dot scanning is generally used to scan the electron beam and then the signal is combined with its location to produce a specific image of the surface of the sample under test [38,39]

Scanning electron microscopy imaging (Complex 2) showed nanoparticles of irregular shapes and sizes, ranging in diameters from 33-334 Nm, and also showed many interstitial distances between minutes, indicating high porosity and high absorbability. As shown figure (7).

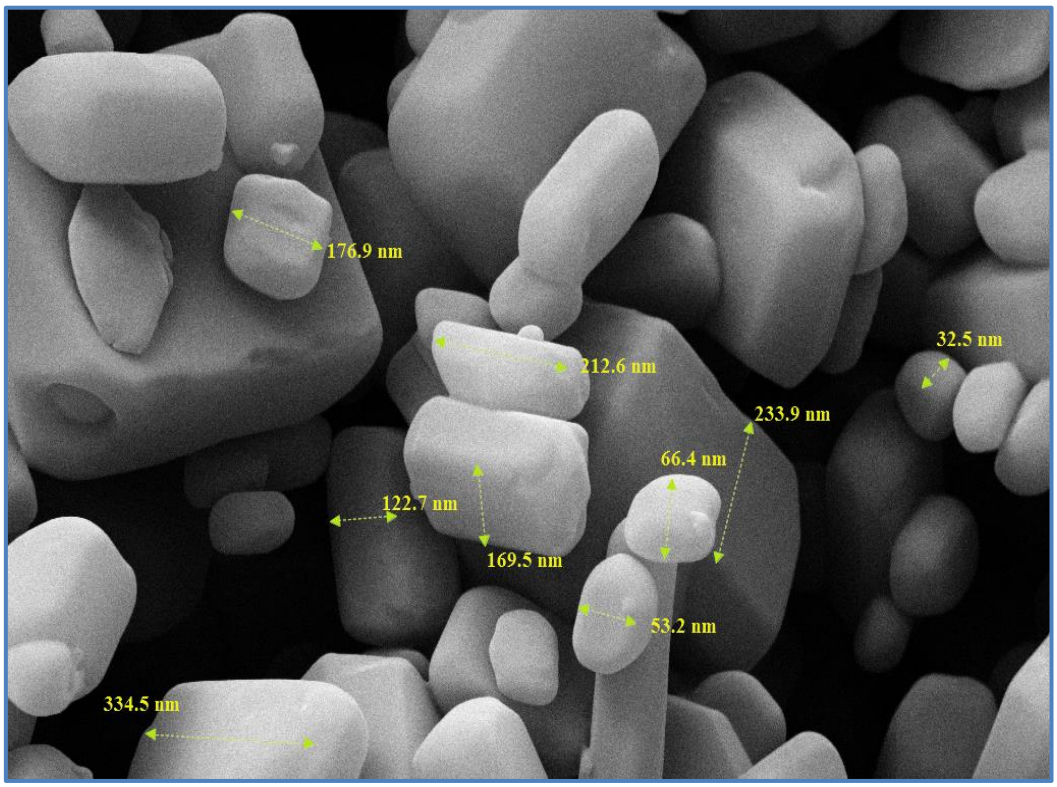


Figure 7. Scanning Electron Imaging of the MH2 Complex

The Results of XRD [40]:

The complex (MH2) has shown beams of high and medium intensity in the diffraction spectrum within the range of 50-10 O, which indicates the presence of a crystal structure of the compound, as well as wide beams, i.e. high FWHM values, indicate the small nanomicrons and high porosity of the complex, which was calculated by the Scherrer equation above and the minute volume rate was equal to(11.44 nm), see Figure (8), Table (1) shows the data of the diffraction spectra of the measured complexes as well as the.

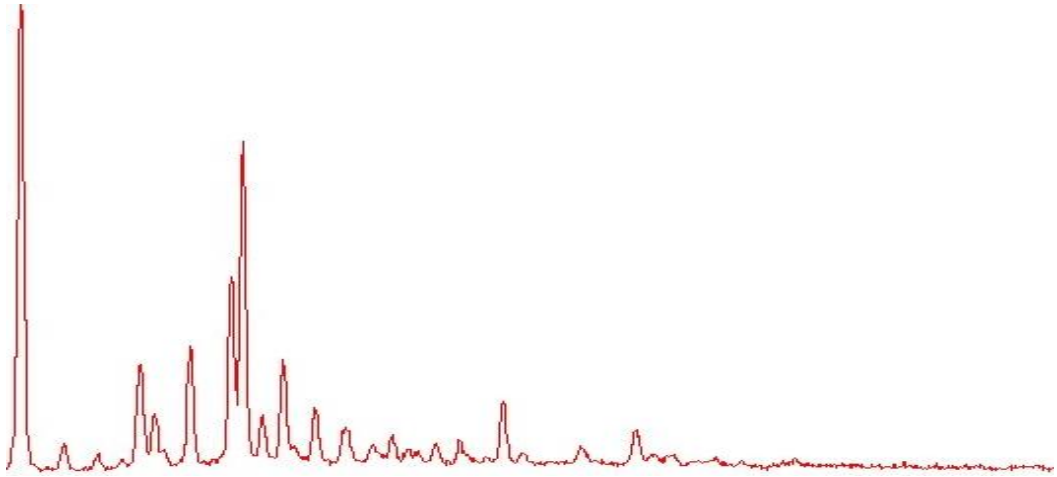


Figure 8. Diffraction Spectra of the Complex (MH2)

Table 1. Data of Doffraction Spectra of the Complex (MH2) as well as the Rate of Minute Volumes According to the Scherrer Equation

Compounds	2θ	FWHM	Intensity	d spacing	D (nm)	Avg. D (nm)
[MM2)]	10.5886	0.3936	180.64	8.35508	21.17653	19.2916
	13.457	1.1808	57.5	6.57993	7.077475	
	18.8696	0.246	269.92	4.70299	34.20054	
	23.6523	0.3444	309.27	3.76172	24.62111	
	25.874	0.3936	141.28	3.44354	21.63536	
	29.3689	0.2952	194.18	3.04122	29.06425	
	41.4743	0.7872	77.29	2.17729	11.27345	
	44.221	1.1808	50.61	2.04822	7.586654	
	48.4092	0.492	109.67	1.88035	18.49489	
	75.5581	0.5904	61.21	1.25843	17.78572	

Evaluation of the Biological Activity:

Certain compounds (MH1, MH2) were evaluated against several bacterial strains using the cup plate agar diffusion method, including gram-negative Escherichia coli and gram-positive Staphylococcus aureus [41, 42, 43]. After eight hours of incubation at 37 °C, the microbial cultures were diluted with 0.8% sterile saline [44,45,46]. The medicines were dissolved in DMSO with a concentration of 100 g/mL. Amoxicillin was employed as a negative control in this experiment. The diameter of the ring encircling the active disk in bacterial growth inhibition was utilized to determine biological activity, as shown in Table (2)[47, 48, 49].

Table 2. Inhibitory Effectiveness of Some Prepared Compound (MH1, MH2) and Control Treatments (Antibiotics) on the Growth of a Number of Positive and Negative Bacteria

Comp. No.	*Escherichia coli*			*Staphylococcus aureus*		
	0.001	0.01	0.1	0.001	0.01	0.1
MH1	23	14	12	30	45	50
MH2	19	26	28	10	25	30
Amoxicillin	10	16	24	10	20	20

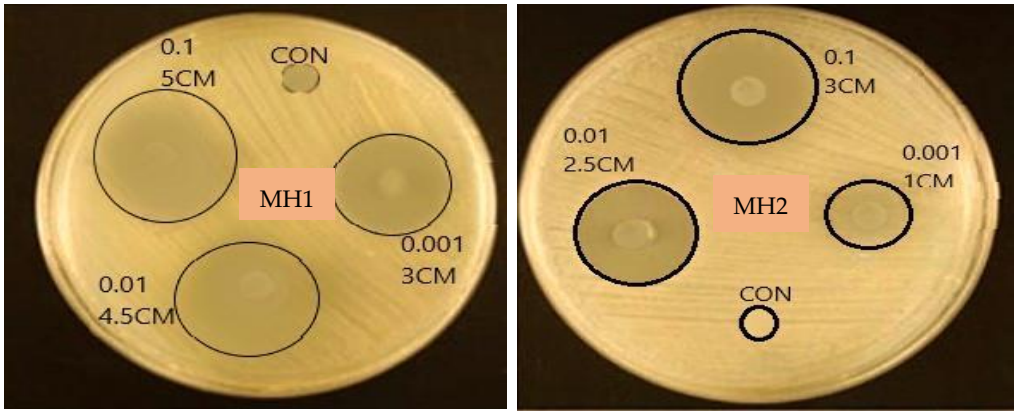


Figure 9. Biological Effect of Some Bacterial of Staphylococcus Aureus and Inhibition Zone for three Concentration

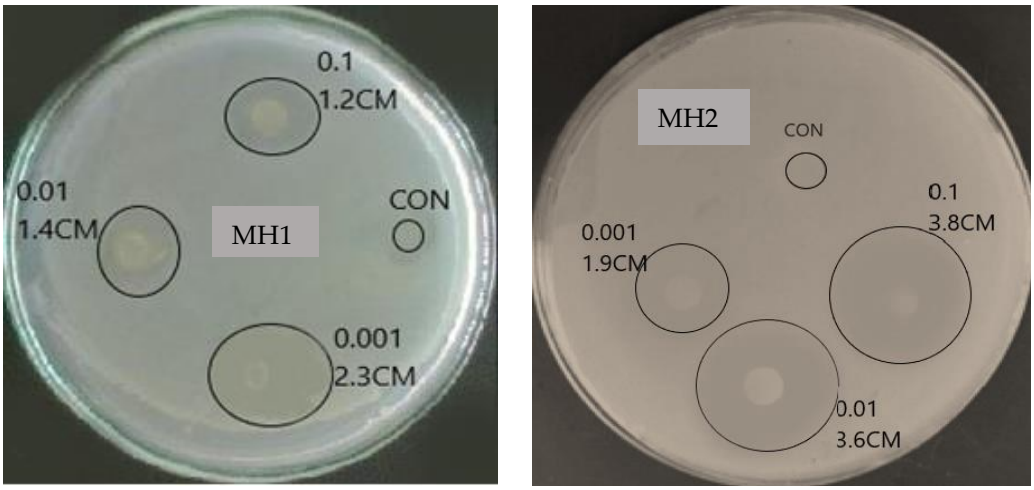


Figure 10. Biological Effect of Some Bacterial of Escherichia Coli and Inhibition Zone for Three Concentration

Results of Molecular Docking Study for MH2 [50]:

The molecular docking of the complex (MH2) was studied on a single line it is a bacterium Pseudomonas aeruginosa, using the MOE program (2014), where the energy reduction process was completed for vehicles under in order to get the most stable vacuum body (the least energy hindrance), then download Synthesis of Pseudomonas aeruginosa bacteria from the World Bank protein site (receptor X3R6), a calculator was used Personality. The binding energy of (MH1) was -4.69, with an RMSD value of 3.13. The binding energy of the complex (MH2) was -6.02, with an RMSD value of 2.08.

The investigation of the molecular adhesion of the revealed the number and types of bonds that these produced derivatives create with amino acid residues in the active site, generating a number of connections.

The study showed that the compound (MH1) interacts with amino acid residues that are present in the active site by forming two types of bonds, hydrogen bonds that bind amino acid residues. 406Tyr is at the active site with the electron pair of the oxygen atom, the carbonyl group with a length of 2.82, and hydrogen bonds that bind the residues of amino acids 331.The Arg is placed in the active site with the electron pair of a sulfur atom with a length of 3.33 and its PI-type interaction with a benzene ring, a number of amino acids impacted by vandervalls forces, and binding energy values of -4.69 were also determined. Figure (11) depicts the findings of molecular anchoring and the interaction of the synthesized chemical MH1 with the receptor X3R6 of a single line of Pseudomonas aeruginosa bacteria.

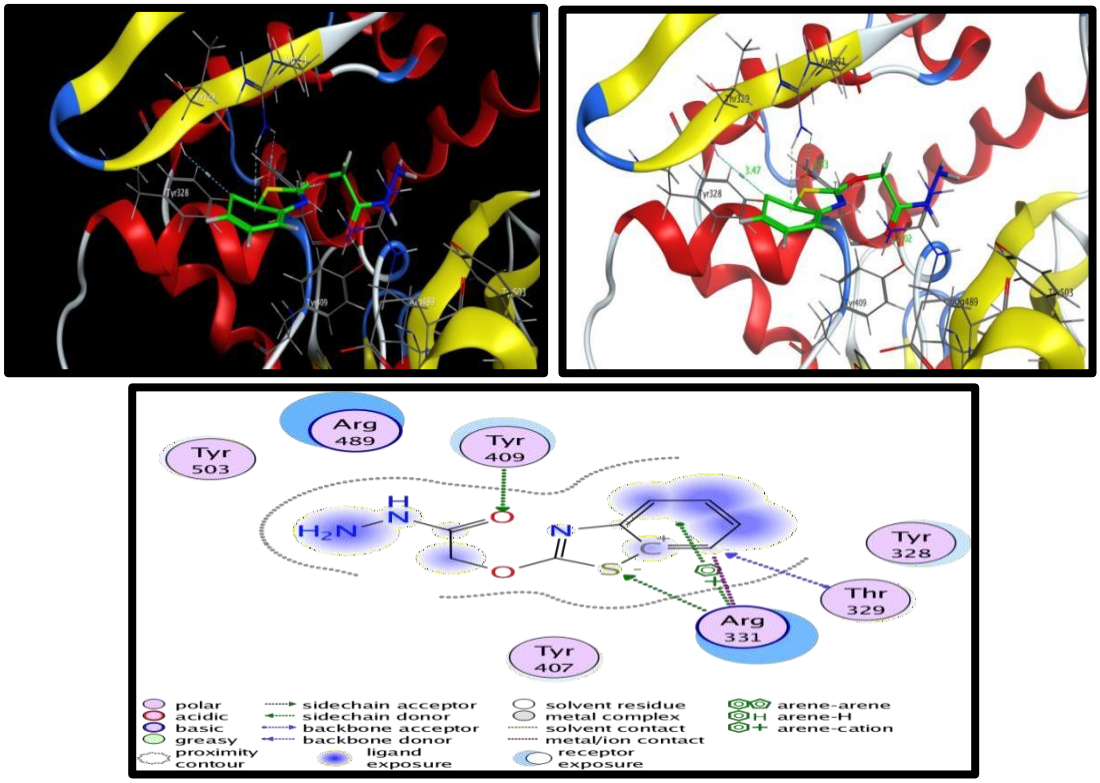
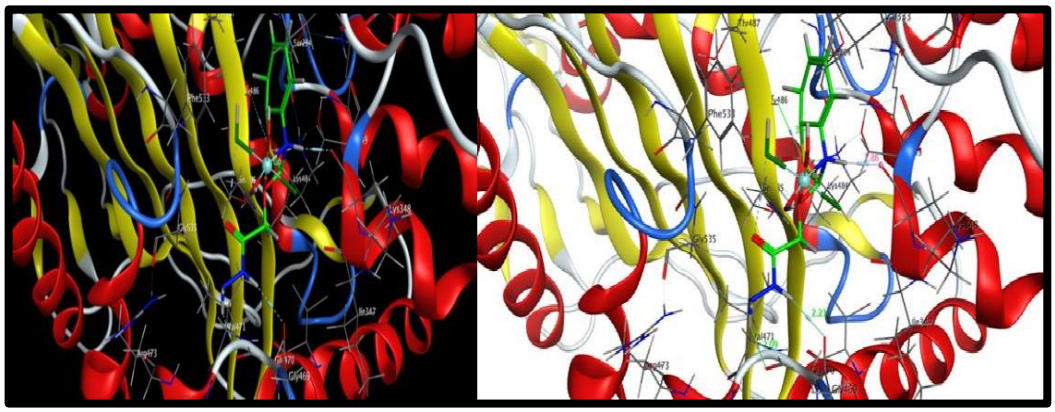


Figure 11. Shows a two-dimensional and Three-Dimensional Representation of the Results of Molecular Docking and the Association Between the Compound (MH1) Prepared Receptor X3R6 Single Line of Pseudomonas Aeruginosa Bacteria

The researchers observed that the chemical (MH2) interacts with amino acid residues in the active site by creating two types of alkyl-Pi ligands that bind to them.487thr, which is at the active site with the aromatic ring's electron pairs and a number of amino acids affected by vandervalz forces, was discovered to have a binding energy of -6.02. Figure 12 depicts a two-dimensional and three-dimensional representation of the molecular docking data, as well as the interaction between the generated chemical (MH2) and the receptor 6X3R one line of the Pseudomonas aeruginosa bacteria.



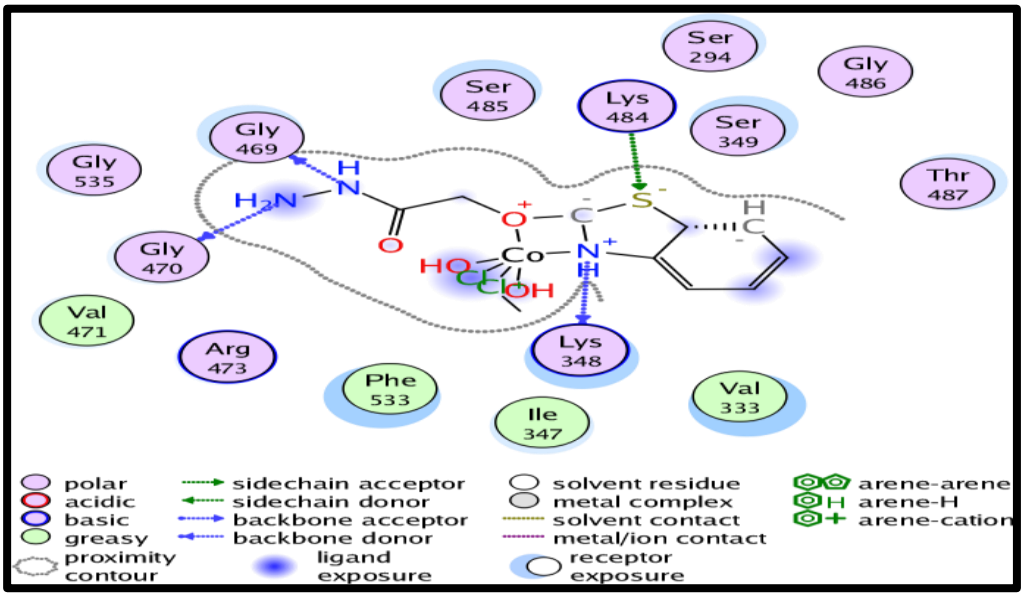


Figure 12. Shows Two-Dimensional and Three-Dimensional Representation of the Results of Molecular Docking and the Association Betweem the Compound (MH1) Prepared Receptor X3R6 Single Line of Pseudomonas Aeruginosa Bacteria

4. Conclusion

The initial confirmation of the prepared compounds was made through color and temperature changes, and the final confirmation was made through the appearance of distinct bands in the FT-IR spectrum, as well as the appearance of the expected signals for the prepared compounds in the C13 H1 NMR spectrum. In addition, the compounds demonstrated strong inhibitory efficacy against bacteria as compared to a control sample.

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