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Synthesis and Biological Activity of a Novel Derivatives of Schiff Base

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Abstract

Since their discovery, Schiff bases have been essential compounds that can be found in nature or synthesized in laboratories. We synthesized new schiff bases (1-3), namely as 4-{(E)-[4-(chloromethyl)phenyl]diazenyl}-2-{[(4-substituted phenyl)imino]-methyl}phenol. These derivatives are synthesized from the 5-{(E)-[4-(chloromethyl)phenyl]diazenyl}-2-hydroxybenzaldehyde and 4-substituted aniline, such as 4-methyl aniline, 4-chloro aniline, and 4-methoxy aniline. Characterization of these compounds by FTIR and ^{1}HNMR spectroscopy. The diffusion method is used to determine how these compounds interact with various bacteria, such as Bacillus subtilis, S. aureus and E. coli. The derivative 2 a good result to inhibition zone of bacteria growth.

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1. Introduction

Imines, or azomethines, also known as schiff bases, have a wide range of applications, including pigments, dyes, and corrosion inhibitors [(1)]. The imine derivatives could have been manufactured through microwave or infrared technology [(2, 3)] and using acid, base, P_2O_5/SiO_2, and $ZnCl_2$ as catalysts [(4)]. Schiff bases play an important role in a variety of biological activities, including antifungal, antibacterial, antimalarial and other application [(5, 6)]. An azo derivative is an organic compound containing an azo group [(7)]. The vast majority of aromatic compound [(8)] are produced by coupling a derivative of diazonium salt with an aromatic compound whose hydrogen atoms can be easily exchanged. Infections brought on via the development of antimicrobial resistance, also known as AMR, to currently available medicines pose an important risk to people's health. AMR-related diseases have been estimated to have killed 4.95 million people in the world in 2019 [(9)]. Furthermore, the rapid spread of multiresistant bacteria around the world is a major problem that requires a quick solution. The extensive and uncontrolled use of antibiotics for human health and animals causes clinical strains and those linked to foodborne infections to become dangerous [(9, 10)]. The need for effective therapies has been the driving force behind the development, production, and research of new biologically active chemicals. According to studies, compared to common chemotherapeutic medicines like cisplatin and doxorubicin [(10)]. To be able to respond to environmental stress, bacteria have developed finely composed responses that, when stimulated, change cellular physiology in a way that improves survival. According to recent studies, controlled modifications in mRNA turnover are essential for bacterial responses to stress [(11)]. In this research, we synthesized a new schiff bases derivatives (1-3) and characterization by different spectroscopic methods and evaluation the biological activity by bacterial zone inhibition.

2. Materials and Methods, or Preliminaries, or Basic Concepts

2.1 Reagents and solvents

All of the chemicals utilized in this study have been obtained from Merck and Fluka.

2.2 Synthesis

2.2.1 Synthesis 5-{(E)-[4-(chloromethyl)phenyl]diazenyl}-2-hydroxybenzaldehyde

In a cooling bath, mix 0.01 mole of 4-chloromethyl aniline with 6 ml of a 10% HCl. Then dissolve (1.38 g of 0.02 mole) of $NaNO_2$ in distilled water. The solution mixture added to the together. Following the filtration of the final solution and collection of the precipitate [13].

2.2.2 Synthesis of schiff base derivatives (1-3) [13, 14]

Dissolve 0.01 mole of an azo derivative in 20 ml of ethanol, then add 3 drops of glacial acetic acid. Added different amine derivatives such as 4-methylaniline, 4-chloro aniline, and 4-methoxy aniline to the solution and refluxed this solution for 3 hours. Filtrated solutions and dry filtration were used to collect crystals.

3. Results and Discussion

The reaction between 2-hydroxybenzaldehyde and 4-chloromethylaniline. The new azo-Schiff base derivatives is yellow colors crystals that synthesized from reaction of azo derivatives as electrophilic and different amine as nucleophilic. Schiff base derivatives have a wide biological activity because of azomethine group that have multi electron on nitrogen atom. The carbonyl of aldehyde and C-H aldehyde appeared at spectrum of FTIR for azo derivative, but disappeare in FTIR specturms for azo-schiff base (1-3) [15, 16].

5-{(E)-[4-(chloromethyl)phenyl]diazenyl}-2-hydroxybenzaldehyde:

Physcial properties: Color: Light yellow. Yield: 68%. Melting point: 167 – 171 °C.
Chemical properties: MWt: 274.70. Formula $C_{14}H_{11}ClN_2O_2$.
FT-IR (KBr, cm^{-1}): 2758 υ(C-H) for aldehyde, 3433 υ(hydroxyl group) [17], 3057 υ(C-H) for aromatic, 2963 & 2875 υ(C-H) for aliphatic, 1710 υ(carbonyl), 1597 (C-C) of aromatic, 1507 υ(azo).
^{1}HNMR (400 MHz, Solvent: DMSO-d_6, ppm) δH: 9.17 (1H, s, Aldehyde), 7.08-7.66 (7H, m, Aromatic) [18, 19], 4.39 (1H, s, CH_2-Cl), 9.37 (1H, s, Ar-OH) (Figs. (1) and (2)).

4-{(E)-[4-(chloromethyl)-2,5-dimethylphenyl]diazenyl}-2-{[(4-methylphenyl)imino]-methyl}phenol: (1)

Physcial properties: Color: dark yellow. Yield: 73%. Melting point: 201 – 205 °C.
Chemical properties: MW: 391.89. Formula $C_{23}H_{22}ClN_3O$.
FT-IR (KBr, cm^{-1}): 3336 υ(hydroxyl) [17], 3071 υ(C-H) for aromatic, 2913 & 2850 υ(C-H) for aliphatic, 1641 υ(imine), 1506 υ(azo), 1604 (C=C) for aromatic.
^{1}HNMR (400 MHz, Solvent: DMSO-d_6, ppm) δH: 9.38 (1H, s, hydroxyl), 7.16-8.08 (9H, m, Aromatic) [19], 2.38 (3H, s, methyl), 4.57 (2H, s, CH_2-Cl), 8.69 (1H, s, imine), [19-20], (Figs. (3) and (6)).

4-{(E)-[4-(chloromethyl)-2,5-dimethylphenyl]diazenyl}-2-{[(4-chlorophenyl)imino]-methyl}phenol: (2)

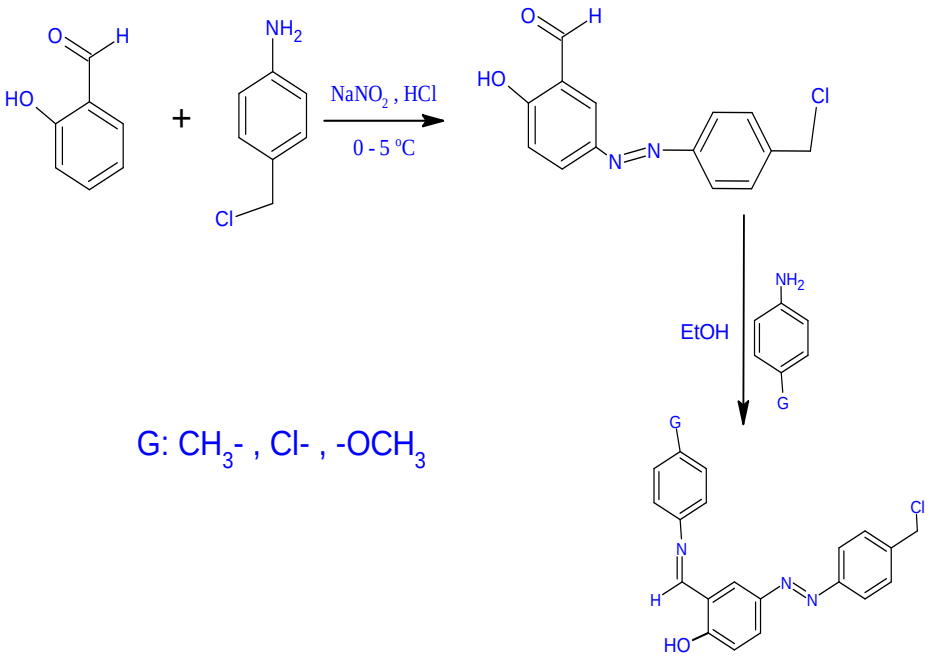
Physcial properties: Color: yellow. Yield: 72%. Melting point: 236 – 240°C. MWt: 412.31. Chemical properties: Formula $C_{22}H_{19}Cl_2N_3O$.
FT-IR (KBr, cm^{-1}): 3296 υ(O-H) [17], 3009 υ(C-H) for aromatic, 2996 υ(C-H) for aliphatic, 1631 υ(imine), 1526 υ(azo), 1585 υ(C=C) for aromatic.
^{1}HNMR (400 MHz, Solvent: DMSO-d_6, ppm) δH: 9.20 (1H, s, hydroxyl), 6.98-8.05 (9H, m, Aromatic) [18, 19], 4.57 (2H, s, CH_2-Cl), 8.69 (1H, s, imine), (Figs. (4) and (7)).

4-{(E)-[4-(chloromethyl)-2,5-dimethylphenyl]diazenyl}-2-{[(4-methoxyphenyl)imino]-methyl}phenol: (3)

Physcial properties: Color: Light yellow. Yield: 64%. Melting point: 212 – 217°C.
Chemical properties: MWt: 407.89. Formula $C_{23}H_{22}ClN_3O_2$.
FT-IR (KBr, cm^{-1}): 3201 υ(O-H) [17], 3022 υ(C-H) for aromatic, 2957 & 2868 υ(C-H) for aliphatic, 1637 υ(imine), 1523 υ(azo), 1588 υ(C=C) for aromatic.
^{1}HNMR (400 MHz, Solvent: DMSO-d_6, ppm) δH: 9.20 (1H, s, hydroxyl), 6.92-7.73 (9H, m, Aromatic), 8.88 (1H, s, imine) [18, 19], 3.80 (2H, s, CH_2-O), (Figs. (5) and (8)).

Biological Activity

Different 50 µg of schiff bases (1, 2, and 3) that have been synthesized as antibacterials were applied to utilize various kinds of bacteria, such as *Bacillus subtilis, S. aureus,* and *E. coli* by the diffusion technique. Schiff base derivative 2 is effective against any available microorganisms bacuse have halide atom more active from other methy and methoxy groups in other compounds synthesized [20, 21]. All results of biological activity listed in table 1 and figure 9.



Scheme 1. Reactions of Synthesized compounds (1 – 3).

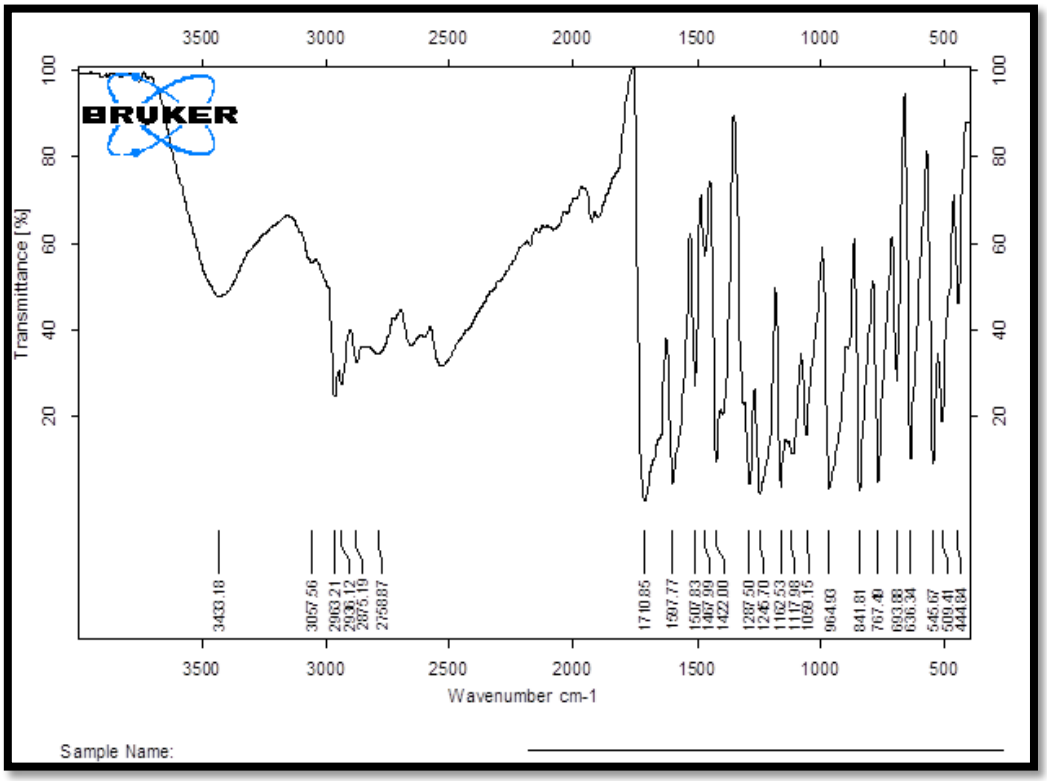


Figure 1. FTIR spectrum for azo derivative.

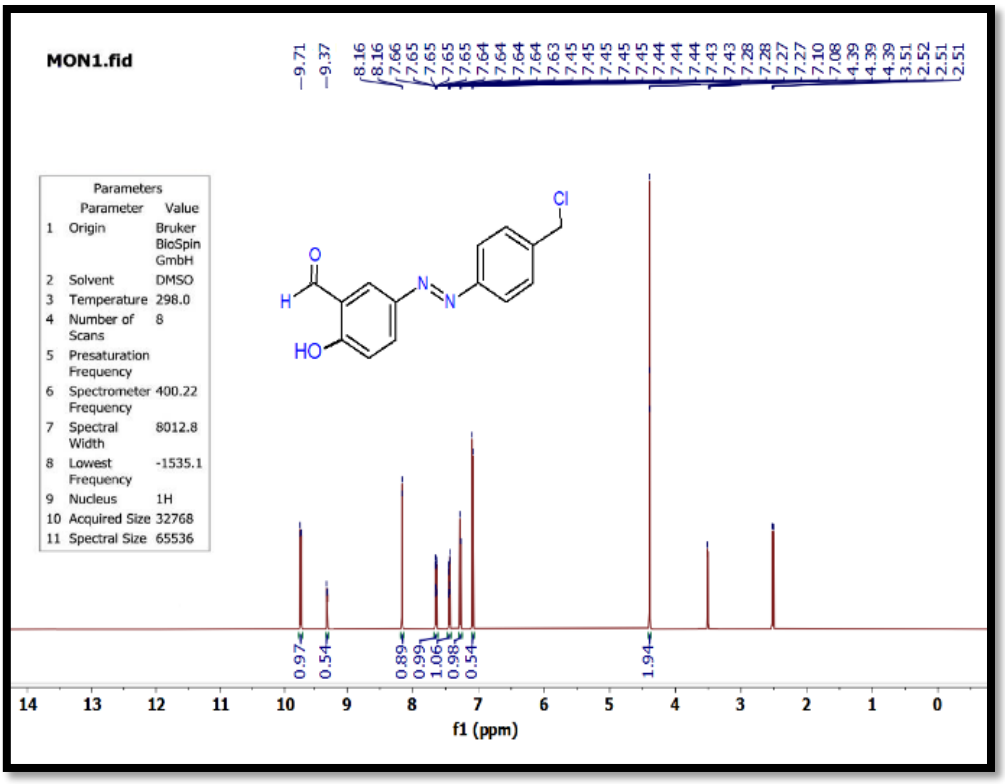


Figure 2. ^{1}HNMR spectrum of azo derivative.

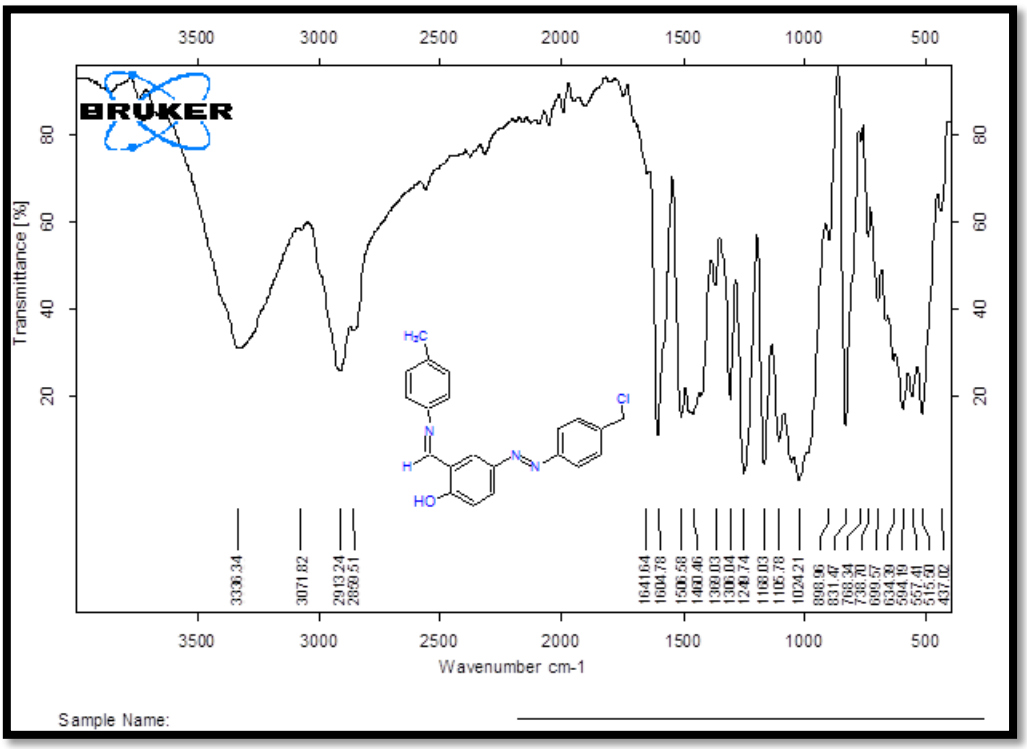


Figure 3. FTIR spectum of derivative 1.

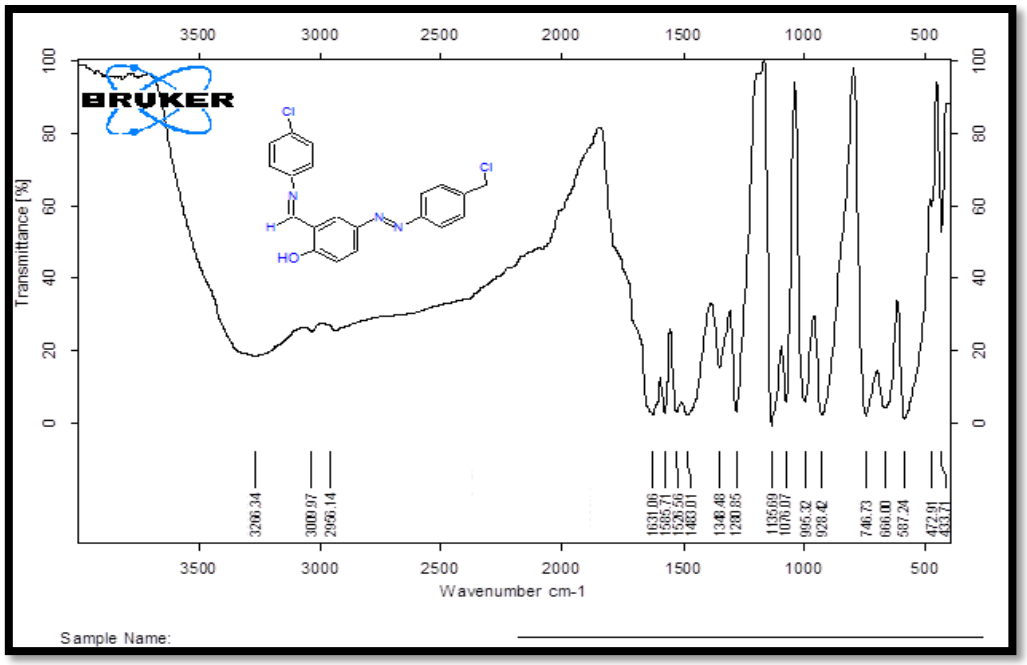


Figure 4. FTIR spectrum of derivative 2.

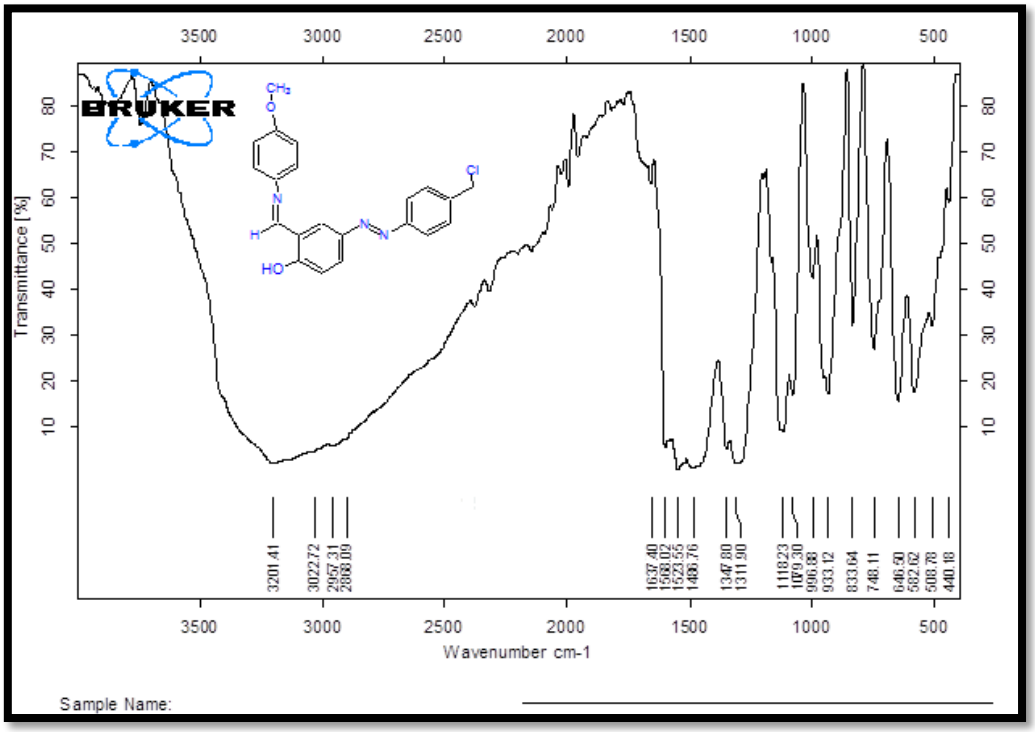


Figure 5. FTIR spectrum of derivative 3.

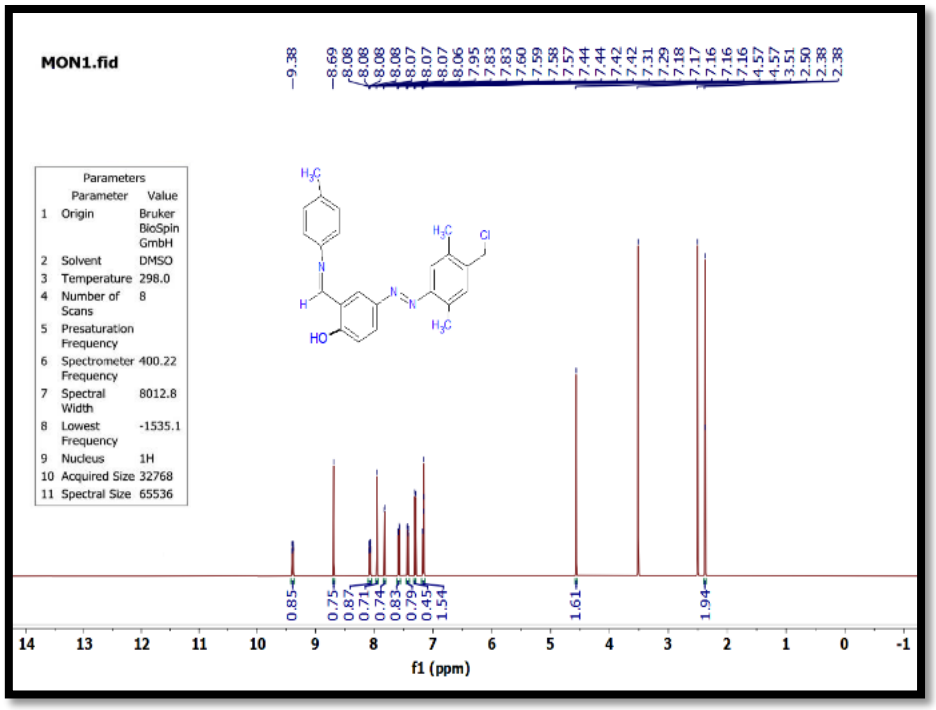


Figure 6. [1]HNMR for derivative 1.

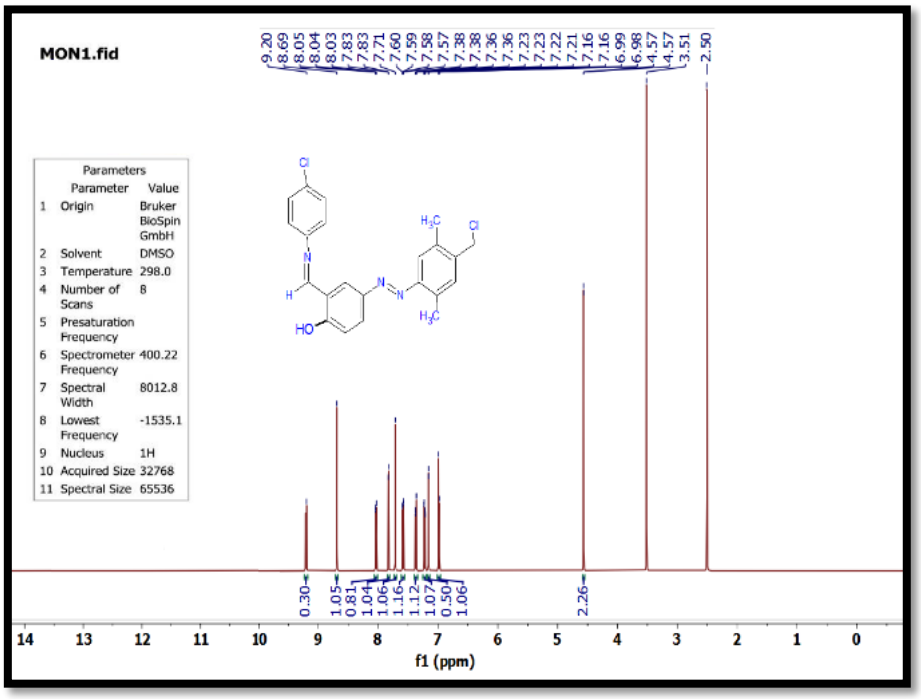


Figure 7. [1]HNMR for derivate 2.

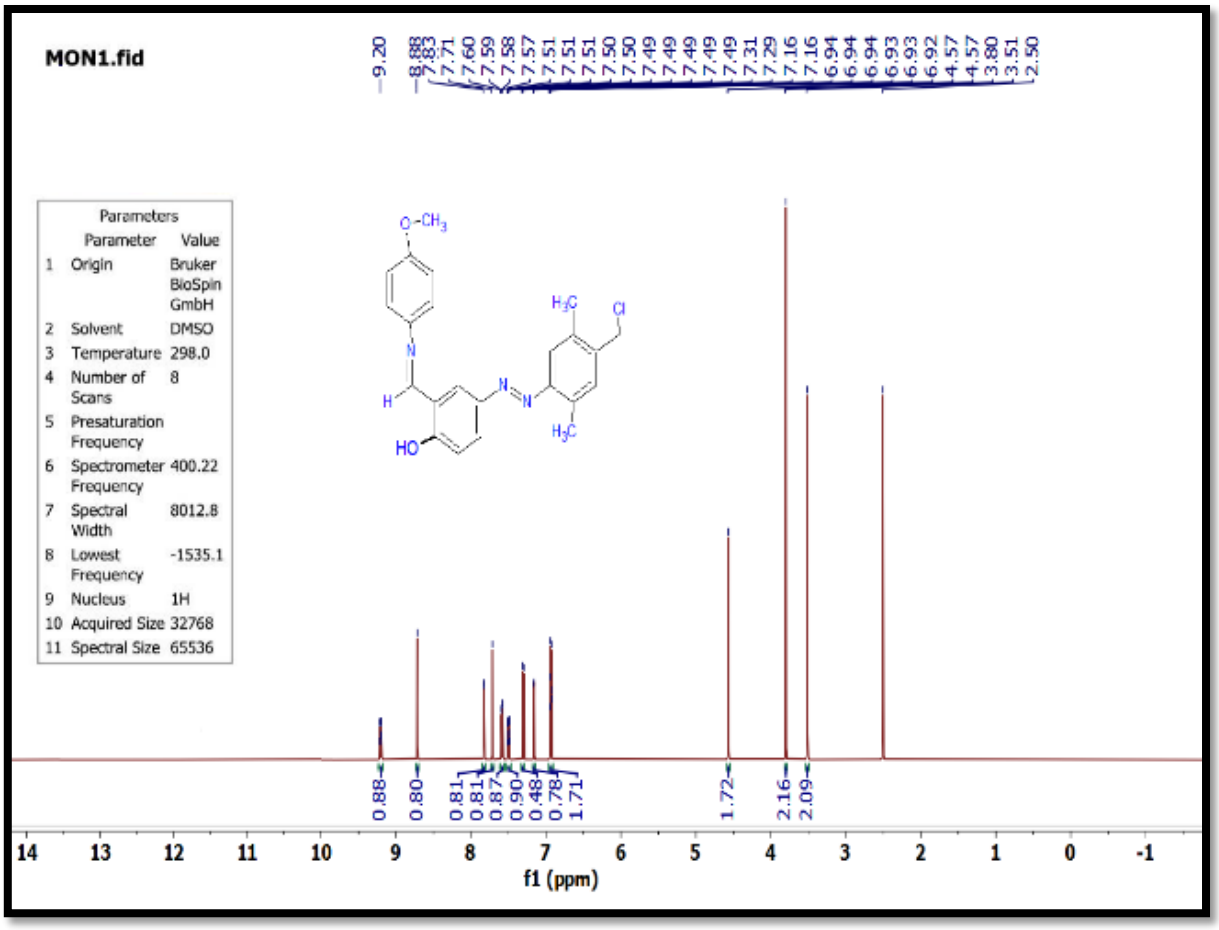


Figure 8. ^{1}HNMR for derivative 3.

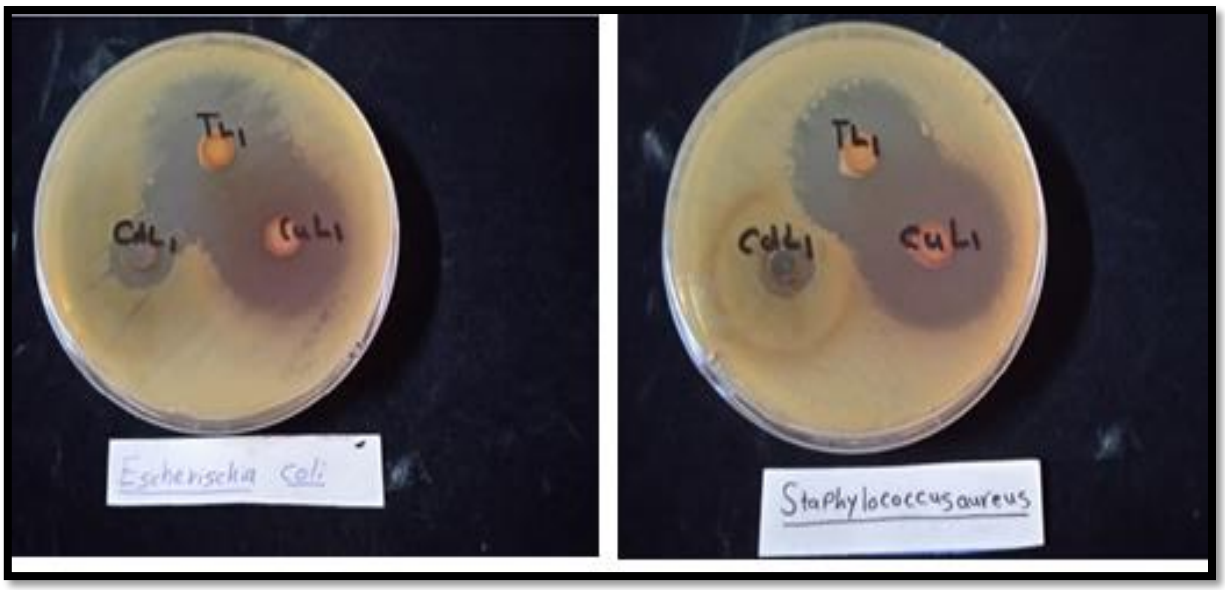


Figure 9. Biological activity of synthesized derivatives.

Table 1. Biological activities for Schiff bases (1, 2 and 3).

Derivative	Zone inhibition (mm)		
	Bacillus subtilis	*S. aureus*	*E. coli*
1	+	+	+
2	+	++	++
3	+	+	+
Note: + was (less 5 mm), ++ was (more 5 mm).			

4. Conclusions

We obtained a novel azo-schiff bases in an easy and speedy way. Upon characterization of these derivatives by ^{1}HNMR and FTIR spectroscopy, the These derivatives (1, 2, and 4) were showed good results as antibacterial against *E. coli, Bacillus subtilis*, and *S. aureus*. The derivative 2 was more activity by zone inhibition of bacteria against all types of bacteria disc. The halide atom such as chlorine in schiff base derivative 2 that give more active because high electronegativity. In future, we synthesized a new derivatives and study molecular docking to explain mechanism of connected between these derivatives and enzymes in bacteria.

References

[1] Ghanghas, P.; Choudhary, A.; Kumar, D.; Poonia, K.; "Coordination metal complexes with Schiff bases: Useful pharmacophores with comprehensive biological applications". Inorg. Chem. Commun., 130 (1), 108710, 2021. https://doi.org/10.1016/j.inoche.2021.108710.

[2] Ceramella, J.; Iacopetta, D.; Catalano, A.; Cirillo, F.; "A review on the antimicrobial activity of Schiff bases: Data collection and recent studies". Anal. Chem., 11(2), 191, 2023.

[3] Qian, C.; Lili F.; Wei Liang T.; Jiawei L.; Weiqaing Z.; "Imine and imine-derived linkages in two-dimensional covalent organic frameworks". Nat. Rev. Drug Disc., 6(12), 881-898, 2022.

[4] Klopcic, I.; Dolenc, M.; "Chemicals and drugs forming reactive quinone and quinone imine metabolites". Chem. Rev., 32(1), 1-34, 2022.

[5] Acharyya, K.; Mukherjee, P.; "Organic imine cages: molecular marriage and applications". Angew. Chem., 131(26), 8732-8745, 2022.

[6] Kudryavtsev K.; Zagulyaeva A.; "1,3-Dipolar Cycloaddition of Schiff Bases and Electron-Deficient Alkenes, Catalyzed by a-Amino Acids.", Springer Ser. Chem. Phys., 44, 378-387, 2008.

[7] Benkhaya, S.; M'rabet, S.; El Harfi, A; "Classifications, properties, recent synthesis and applications of azo dyes". Helv. Chim. Acta, 6 (1), 271, 2020.

[8] Przybylski, P.; "Biological properties of Schiff bases and azo derivatives of phenols". Curr. Org. Chem., 13 (1), 143, 2009.

[9] Pasquier, N.; Keul, H.; Heine, E.; "From multifunctionalized poly (ethylene imine) s toward antimicrobial coatings". Biol. Chem., 8 (9), 2874-2882, 2007.

[10] Iacopetta, D.; Jessica C.; Alessia C.; Alessia C.; Carlo F.; Maria S.; "Schiff bases: Interesting scaffolds with promising antitumoral properties". Appl. Catal., 11(4), 1877, 2021.

[11] Anderson, K.; "Messenger RNA turnover processes in Escherichia coli, Bacillus subtilis, and emerging studies in Staphylococcus aureus". Int. J. Inorg. Mater., 54 (12), 57,2009.

[12] Benkhaya, S.; M'rabet, S.; "Classifications, properties, recent synthesis and applications of azo dyes". Helv. Chim. Acta, 6(1), 271, 2022.

[13] Shah, D.; Brahim K.; Sajjad A.; Umar A.; "Synthesis and antioxidant activities of Schiff bases and their complexes: An updated review". Rev. Anal. Chem, 10 (9), 6936-6963, 2021. https://doi.org/10.33263/BRIAC106.69366963.

[14] Segura, J.; Mancheño, M.; "Covalent organic frameworks based on Schiff-base chemistry: synthesis, properties and potential applications". Chem. Soc. Rev., 45(20), 5635-5671, 2016.

[15] Reda S.; Salih A..; "Mn(II),Fe(III),Co(II)and Rh(III) complexes with azo ligand: Synthesis, characterization, thermal analysis and

bioactivity". Bagh. Scie. J., 20(3): 2774-2785, 2023.
[16] Thirunavukkarasu, T.; Sparkes, H.; Natarajan, K.; "Synthesis, characterization and biological studies of a novel Cu (II) Schiff base complex". Inorg. Chem. Commun., 473, 255-262., 2018.
[17] Sharma, Y.; "Elementary organic spectroscopy". Chan. Publ., 23(4), 253, 2007.
[18] Ani, F.; Friday E.; Collins U.; Nnamdi L.; Monsuru T.; Kingsley U.; Gideon F.; Segun A.; "Crystal, spectroscopic and quantum mechanics studies of Schiff bases derived from 4-nitrocinnamaldehyde". Sci. Prog., 11 (1), 8151, 2021.
[19] Saritha, T.; Metilda, P.; "Synthesis, spectroscopic characterization and biological applications of some novel Schiff base transition metal (II) complexes derived from curcumin moiety". J. Saud. Chem. Soci., 25 (6), 101245, 2021.
[20] Liu, Y.; Longrui W.; Dawei Y.; "Solvent-free synthesis, characterization, biological activity of schiff bases and their metal (II) complexes derived from ferrocenyl chalcon". Org. Process Res. Dev., 899 (1), 120903, 2019.
[21] Omidi, S.; Kakanejadifard, A; "A review on biological activities of Schiff base, hydrazone, and oxime derivatives of curcumin". Rev. Anal. Chem, 10 (50), 30186-30202, 2020.