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Original Research Article

Synthesis, Characterization and Biological Study of New Schiff Bases

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Abstract And Objective: The synthesis of Schiff base compounds has garnered significant attention recently due to their importance and applications across various fields, especially because of the presence of an azomethine group. Schiff bases have been utilized as intermediates in the synthesis of new organic compounds. Given their biological and pharmacological activities, we aimed to prepare new compounds in this study to develop biologically active substances that could serve as lead compounds. ***Methods:*** Two series of Schiff base compounds (3a-f and 6a-e) were synthesized through the reaction of equal moles of various substituted benzaldehydes and heterocyclic aldehydes with amine compounds (1). The second series (6a-e) were prepared from the reaction of 3-Nitrobenzyloxy benzaldehyde with different aromatic amines. This was achieved using the condensation method under reflux conditions. ***Result:*** The synthesis of 3-nitrobenzyloxybenzaldehyde was accomplished through the Williamson ether synthesis method. , involving the reaction of 4-hydroxy benzaldehyde with 3-nitrobenzyl chloride in the presence of K_2CO_3. This compound was utilized as a substituted benzaldehyde in the preparation of Schiff base compounds (6a-e). The resulting products were characterized based on their physical properties and through various analytical techniques, including infrared (IR) spectroscopy, as well as proton nuclear magnetic resonance (1H-NMR) spectroscopy and carbon-13 nuclear magnetic resonance (13C-NMR). We assessed the antibacterial activities of all synthesized compounds against two types of bacteria Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli. ***Conclusion:*** The Schiff bases derived from compound (1) demonstrated enhanced antibacterial activity against both gram-negative and gram-positive bacteria compared to the series (6a-e).

Keywords: Schiff base, 3-Nitrobenzyloxybenzaldehyde, 3-aminoacetophenone, Antibacterial activity

INTRODUCTION

The condensation of primary amines and carbonyl compounds results in the formation of a Schiff base. A Schiff base is characterized by the general formula $R^1R^2C{=}N\text{-}R$ and is also referred to as an imine. Recently there has been great interest in the synthesis of Schiff base derivatives due to their application in different fields, such as their importance in pharmaceutical and biological fields[1,2], the synthesis of some Schiff's base improves drug discovery efforts for Alzheimer's potentially improving patient outcomes, showed anticancer activity and their use as intermediates in the synthesis of different aromatic compounds.[3] The presence of an azomethine bond (N=CH) and the lone pair of the nitrogen atom, along with heterocyclic in one molecule, it often boosts how well the compound works biologically.[4].

Our aim of this study is to synthesize the new compounds including heterocyclic moiety. Heterocyclic compounds have several applications, including agrochemical and pharmaceutical.

The significance of heterocyclic compounds has been recognized in the synthesis of copolymers. These compounds are present in various applications, including sanitizers, antioxidants, dyestuffs, and corrosion inhibitors.[5] Schiff bases that incorporate heterocyclic moieties have demonstrated physiological and pharmacological activities, highlighting their potential in the development of new drug derivatives. Additionally, many natural compounds, antibiotics, and pharmaceuticals contain heterocyclic rings within their structures.[6]

For example some marketed drugs including heterocycles and azomethin bonds in their structures, are Dantrolene®, Nitrofurantoin® and Nifurtimax,There are other example of Schiff bases that showed antibacterial activity ,antioxidant activity and acted as potent urease inhibitor.[7]

MATERIAL AND METHODS

This study was conducted at college of pharmacy / Hawler medical university between 1 of October 2024 to 30 of June 2025, by using different substituted aromatic aldehydes, and heterocyclic aldehydes and two types of amine 2(4-aminophenyl)-6-methylbenzothiazole and 3-aminoacetophenone. Electrothermal melting point apparatuses from Stuart Scientific was used for determination of melting points (Table 1). The infrared spectra were recorded using A spectroscopy –specific Jasco FT-IR 4600 Spectrometer at the college of pharmacy/ Hawler medical university. ^{1}H-NMR and ^{13}C-NMR spectra were measured using a Bruker 400 MHz with internal TMS as reference (Day petronic Company, Iran) and NMR: Bruker analytic, 400MHz, Photon Center for Nano Development and Research.

Synthesis of 3-Nitrobenzyloxy benzaldehyde[8]

6.106 g (0.05 mol) of 4-hydroxybenzaldehyde dissolved in 5ml ethanol and 15.203 g (0.11 mol) of K_2CO_3 were dissolved in 5 ml of absolute ethanol mixed , stirred at room temperature for 2 hours. Afterward, 8.579 g (0.05 mol) of 3-nitrobenzyl chloride was added to the mixture, which was then heated under reflux for 7 hours. Following the heating, the mixture was cooled, treated with ice, and recrystallized using a suitable solvent.

A general method for synthesis of Schiff bases compounds (3a-d) [9]

The synthesis involved dissolving and mixing of substituted aromatic aldehydes (0.01 mol) in 10ml of absolute ethanol with (1.3516 g 0.01 mol) of 3-aminoacetophenone in absolute ethanol (10 mL) and adding 2 to 3 drops of glacial acetic acid to acidify it as catalyst. The mixture was heated under reflux conditions for 6 to 8 hours. The reaction process was monitored using thin layer chromatography (TLC). After cooling, recrystallization was performed with an appropriate solvent. The physical properties of the resulting compound are summarized in Table 1.

Synthesis of (*E*)-3-(((3-acetylphenyl) amino) methylene)-2-ethoxychroman-4-one (3e)[10] Ethanolic solution of 4-H-1-Benzopyran -3-carbaldehyde (1.74.15g,0.01mol) and (1.3516 g ,0.01 mol) of 3-aminoacetophenone were mixed together and stirred for 3hr at 30-35 ºC, after that cooled to room temperature. The yellow precipitate was filtered off and recrystallized from ethanol. The physical properties are described in Table 1

Synthesis of Schiff bases of compounds (6a-e)[8]

0.01 mol of 3-nitrobenzyloxybenzaldehyde was dissolved in 10 mL of absolute ethanol and then mixed with a solution containing 0.01 mol of amine compounds. The resulting mixture was heated under reflux conditions for 6 to 7 hours and subsequently cooled to room temperature. After cooling, the mixture was filtered and recrystallized using absolute ethanol. The physical properties are detailed in Table 2.

Antibacterial study

The antibacterial activity of the Schiff bases was studied using the well diffusion method.[11-12]
against two types of bacteria, gram-positive *S. aureus* and gram-negative bacteria *E. coli.* We performed the well diffusion test by making nutrient agar plates and adding a specific amount of bacteria to them. Muller-Hinton agar and nutrient agar were used for the preparation of medium for maintenance of pure culture. Using a clean loop, we spread a standardized bacterial culture on the nutrient agar plates, and we tested three different concentrations 250 µg/ml,500 µg/ml ,1000 µg/mlof each compound mixed in DMSO. A sterile cork borer (8 mm) was used to prepare cups constructed on petri plates, each well filled with 0.1 ml of each tested compound .We then incubated the bacterial plates at 37°C for 24 hours. The assessment of antibacterial activity was done by measuring the diameter of clear zones of inhibition in millimeters.

RESULTS

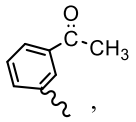
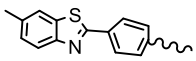
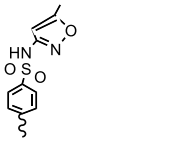
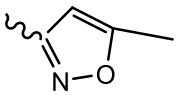
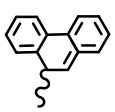
Two series of Schiff bases were prepared, specifically compounds 3a-f and 6a-e. The initial step of this research involved synthesizing Schiff bases derived from 3-aminoacetophenone (1). All synthesized compounds were obtained as powder, crystallized from an appropriate solvent, and yielded satisfactory results. The subsequent step focused on synthesizing Schiff base compounds derived from 3-Nitrobenzyloxy benzaldehyde (4). The comprehensive preparation of compounds 3a-f and 6a-e demonstrates effective methodologies and underscores the robustness of the employed processes, as indicated by their satisfactory crystallization yields. This study not only contributes to the current collection of Schiff bases but also opens avenues for further exploration of their potential applications across various scientific fields. The insights gained from this research establish a solid foundation for future investigations into the properties and functionalities of these versatile compounds. Additionally, 3-nitrobenzyloxy benzaldehyde was synthesized using the Williamson ether synthesis method, which involved the reaction of 4-hydroxy benzaldehyde with 3-nitrobenzyl chloride in the presence of K_2CO_3. This compound served

as the substituted benzaldehyde in the preparation of Schiff bases for compounds 6a-e. The melting points, percentage yields, and other physical properties are presented in Tables 1 and 2.

Table 1: Some physical constants of the synthesized compounds (3a-f)

Compound No.	R	Chemical Formula	M.p C°	Yield %	Color
1			94-98		
3a	3-NO2	$C_{15}H_{12}N_2O_3$	1453-145	67	Beige
3b	4-Cl	$C_{15}H_{12}ClNO$	142-143	59	White
3c	4-OH	$C_{15}H_{13}NO_2$	226-227	63	Light yellow
3d	4-NO_2	$C_{15}H_{12}N_2O_3$	119-120	75	yellow
3e	4-Oxo-4-H-1-benzopyrane-3-CHO	$C_{17}H_{13}NO_3$	178-179	30	yellow
3f	2-Bromo3-pyridine-3-CHO		267d	*56*	*Red*

Table 2: *Some physical constants of the synthesized* compounds (6a-e)

Compound No.	Ar-	Chemical formula	MP °C	Yield %	Color
4	3-NO_2-C_6H_4-C_6H_4CHO	$C_{14}H_{11}NO_4$	53-56	80	Yellow
6a		$C_{22}H_{18}N_2O_3$	106-108	40	White
6b		$C_{27}H_{21}N_3SO_3$	264-265	65	Green
6c		$C_{23}H_{17}N_4SO_{56}$	195-200	82	Yellow
6d		$C_{17}H_{14}N_3O_4$	163-164	75	White
6e		$C_{28}H_{20}N_2O_3$	148-150	60	Dark pinkish

The formation of Schiff bases was confirmed by the disappearance of the characteristic carbonyl group band of the aldehyde compounds at 1689-1693 cm^{-1}, along with the two peaks of the amino group (NH_2) observed at 3460, 3285cm^{-1}. These peaks correspond to the symmetric absorption bands of both amine compounds, confirming the reaction of amines in compounds 1 and 4 with the aldehyde compounds. New peaks associated with the azomethine (CH═N) group characteristic vibration appeared in the region between 1573 and 1627 cm^{-1} for compounds 3a to g, while the IR spectra of compounds 6a to g showed this peak at 1581-1631 cm^{-1}, indicating the successful formation of the desired compounds. The vibration frequency of the carbonyl group (C═O) in compounds 3a-g was noted at 1658-1673 cm^{-1}. Absorption in the range of 2850 to 2981 cm^{-1} corresponded to C-H aliphatic, whereas C-H aromatic absorption was observed at 3050-3179 cm^{-1}.

Table (3): The FTIR spectral data presents the characteristic frequencies of the synthesized compounds, measured in cm^{-1}.(3a-f)

Compound No.	υNH	υC-H aromatic	υC-H aliphatic	υC=O	υC=N	υNO_2 as. str.	υNO_2 s. str.
1	3463 3263	3050	2977	1662			
3a		3070	2977	1673	1627		
3b		3050	2935	1658	1592		
3c							
3d		3070	2981	1666	1573		
3e		3081	2973 2904	1681 1643	1581		
3f				1673	1592		

Table (4): Assignment of characteristics frequencies υ (cm^{-1}) of IR spectral data of the synthesized compounds(6a-e)

Compound No.	N-H	C-H Ar ali	C=O	CH=N	C=C	NO_2 assym.	NO_2symm.	C-O
4		3066 2962 2919	1681	The	1446	1515	1338	1241
6a		3066,	1677	1600	1423	1515	1346	1253
6b		3089 2900		1581		1523	1346	1253
6c	3259	3158 2900		1608	1469	1523	1380	1253
6d		3077		1604	1434	1523	1349	1253
6e		3073 3000 2857		1631	1450	1527	1342	1257

Table 5: The ^{1}H-NMR spectral data for some of the synthesized compounds(3a-e), and (6a-e)

Compound	Chmical shift δ (ppm)
3a	^{1}H-NMR(DMSO-d_6) : 2.6(s,3H,CH_3) 7.6-8.7 (m,,8H,Ar), 8.9 (s,1H, CH=N).
3c	^{1}H-NMR(DMSO-d_6): 2.64,(3H,CH_3)6.83-7.69(m,8H,Ar), ^{1}H-NMR(DMSO-d_6): 9.49(s1H,C=N), 9.95(s,1H,OH),
3e	^{1}H-NMR(DMSO$d_6$1(t,3H,CH_3),2.63(s,3H,CH_3)3.7(q,2H,CH_2), 7-8.26(m,9H,Ar), 11.9(d,1H,NH)
6a	^{1}HNMR(DMSO-d_6) 2.63 (s,3H,CH_3),5.35(s,2H),7.19-8.35(m,12H,Ar),8.61(s,1H,CH=N)
6c	^{1}H-NMR(DMSO-d_6) 2.32 (s CH_3), 5.4 (s,2H,CH_2),6.20(s,1H,CH,ioxazole ring),7.20-8.56 (m,12HAr), 8.36(CH=N),11.46 (s,1H,NH),
6d	^{1}H-NMR(DMSO-d_6) 2.42 (s CH_3), 5.39 (s,2H,CH_2),6.49 (s,1H,CH,ioxazole ring) 7.20-8.56 (m,8HAr),8.32(CH=N)

S=singlet, d=doublet, t= triplet, m = multiplet

Table (6): The^{13}C-NMR Spectral data of some of the synthesized compounds

Compound No.	Chmical shift δ (ppm)
3a	^{13}C-NMR(DMSO)198.24(C=O), 160.66 (C=N), 151.36(C-N), 148.56(C-NO_2),

3c	138.41(C-C=O)(Ar),137.82(Ar), 131.05(Ar), 130.83(Ar), 130.22(Ar) 123.45(Ar),126.39(Ar), 126.72(Ar), 126.57(Ar), 121.12(Ar), 27.42(1C, CH3), ^{13}C-NMR(DMSO):209 (C=O), 160.41(C-OH), 160.4(C=N), 155.35(C-N),152.19(C-C=O ,Ar), 135.22(Ar), 129.32(Ar),127.10,124.71(Ar),117.51(Ar),116.07,36.10(CH_3).
3e	^{13}C-NMR(DMSO) 198.09,(C=O), 180.72(C=O), 156.11(Ar), 145.32(Ar), 140.67(=CH), 138.65(Ar)138.43 (Ar), 135.00(Ar), 130.51(Ar), 126.11(Ar), 123.97(Ar), 123.04(Ar), 122.35(Ar), 121.76(Ar), 118.51(Ar), 116.34(C-Pyran), 104.52(Ar), 100.52 (C-H,Pyran), 63.51(CH_2O),27.40(CH_3) , 15.48(CH_3)
6a	^{13}C-NMR(DMSO) 198.29(C=O), 161.43 (ArC-O), 161.229C=N), (152.50 , 148.32, 139.49, 138.35, 134.60, 131.19, 130.57, 130.03, 129.72, 126.23, 125.71, 123.33, 122.58, 120.91, 115.63)Ar, 68.59(CH_2O), 27.68(CH_3)
6c	^{13}C NMR (DMSO) δ 170 C-O (isoxzazole),162.87ArC-O, 161.CH=N,158.45Ar-N, , 148.33C-NO_2, 139.42, 139.16, 136.28, 134.66, 134.60, 132.32, 131.50, 130.57, 129.12, 123.34, 122.60, 122.10, 115.71, 95.84,C-H)(isoxazole),68.63CH_2)(, 12.53 (CH_3).
6d	^{13}C NMR (DMSO) δ 171.01 C-O Isoxazole ring ,170.1 C-OCH_2 166.04 N=CH, 162.01C=N Isoxazole ring, 148.3 C=NO_2, 139.39 C-CH_2, 134.69 Ar,131.77 Ar, 130.63 Ar, 128.87Ar, 123.40Ar, 122.67Ar, 115.82 Ar, 95.75 C-H Isoxazole ring , 68.68CH2-, 12.85 CH_3.

Antibacterial study

The antibacterial activity of the Schiff bases was studied using the well diffusion method.[11-13]

Choosing two kinds of bacteria, gram-positive *S. aureus* and gram-negative bacteria *E. coli.* We performed the well diffusion test by making nutrient agar plates and adding a specific amount of bacteria to them of each compound mixed in DMSO. The assessment of antibacterial activity was conducted by measuring the diameter of clear zones of inhibition in millimeters. he negative control used was DMSO, while the positive control was ciprofloxacin. The synthesized compounds were evaluated in comparison to ciprofloxacin and amikacin. Ciprofloxacin demonstrated greater activity compared to the synthesized compounds. Additionally, the synthesized compounds exhibited higher reactivity against *E. coli* than against *S. aureus*. However, compound 6e showed no reactivity. The antibacterial result of amikacin was closest to that of the synthesized compounds.

Table (7): The diameter of inhibition zones in millimeters of the synthesized compounds (3a-g and 6c-g)) for assaying the antibacterial activity.

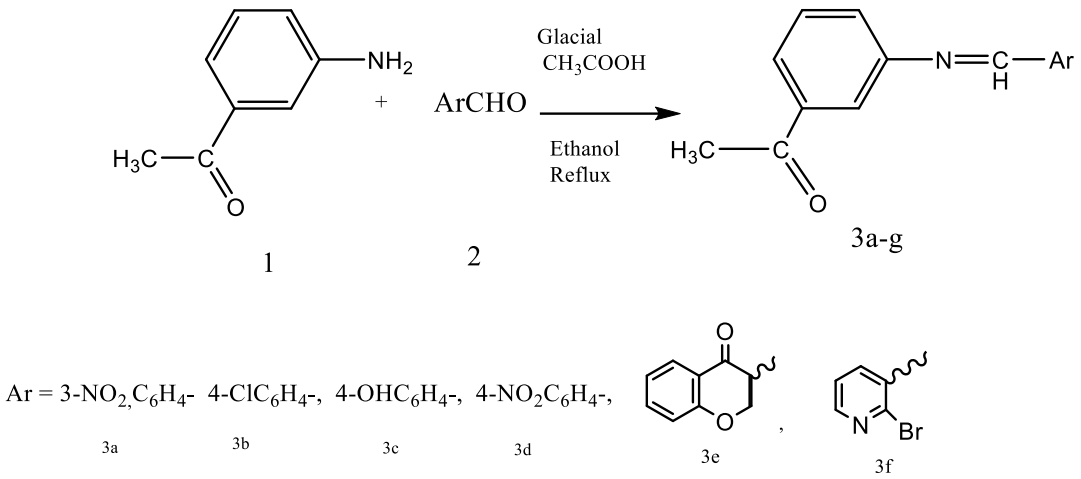
.Compound	*S.aureus* ATCC 25923			*E.coli* ATCC 35218		
compound	1000µg	500µg	250 µg	1000µg	500µg	250µg
3a	++	+	+	+	+	++
3b	+	+	+	++	+	+
3c	++	+	+	++	++	+
3d	++	+	+	+++	+	++
3e	+	+	+	+	+	+
6a	+	+	+	+	+	+
6c	++	+	+	+++	++	+
6d	+	+	+	+	+	+
6e	NIZ	NIZ	NIZ	NIZ	NIZ	NIZ
Amikacin	12-15mm	12-15	12-15	13-19	13-19	13-19
Ciprofloxacin	34mm	30mm	27mm	45mm	43mm	37mm

Zone of inhibition after 24 hrs, zone size 10-14 mm = + 15-19 mm = ++ , 20-25 = +++

DISCUSSION

The first step of this work was the synthesis of Schiff bases derived from 3-aminoacetophenone (1) The traditional method of condensation reaction, which involves reflux conditions and the use of glacial acetic acid as a

catalyst, was applied to various substituted aromatic aldehydes, however, the heterocyclic aldehydes reacted at lower temperature. The Schiff base was synthesized successfully and characterized based on its physical properties using instrumental techniques such as IR, ^{1}H-NMR, and ^{13}C-NMR, as illustrated in Scheme 1



Scheme 1: Synthesis of 1-(substituted benzylidene)3-amminoacetophenones derivatives(3a-F)

Spectroscopic analysis of compound 3a Figure (4) presents the IR spectrum of compound 3a, emphasizing an absorption band at 1623 cm^{-1} corresponding to the imine CH=N bond. Notably, there is a disappearance of the symmetric stretching vibration of the amine (N-H) at 3463 and 3263 cm^{-1}, as well as C-H stretching in the aromatic region at 3070 cm^{-1}. Furthermore, the carbonyl (C=O) absorption in the Schiff base is observed at a higher frequency of 1677 cm^{-1}. Table (3). The ^{1}H-NMR spectrum in DMSO of all of the compounds showed signals related to the solvent at δ 2.5 ppm and δ 3.3 ppm for the water of the solvent, the compound 3a Figure (7) reveals a singlet signal for the CH_3 group of acetophenone at δ 2.64 ppm, and a multiplet of 8 protons in the aromatic region from δ 7.66 to 8.7, attributed to the presence of two phenyl rings. The singlet at δ 8.913 ppm, which corresponds to the CH=N bond, confirms the formation of the desired product.

The ^{13}C-NMR spectrum analysis of compound 3a (Figure 3) displayed a signal at δ 27.42 ppm corresponding to CH_3 group, along with 12 signal for the two phenyl groups in the aromatic region at δ 121.12-151.36 ppm; additionally, the carbons of the azomethine group (C=N) and carbonyl (C=O) appeared at δ 160.66 and 198.24 ppm, respectively. Figure 7, Table 5 and 6

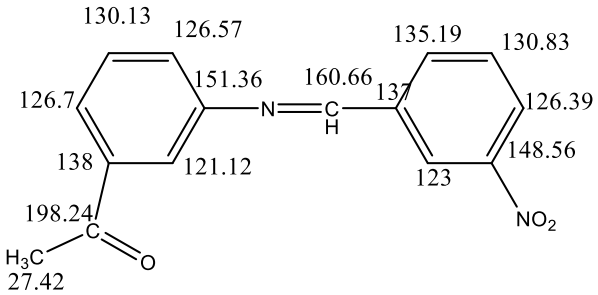


Figure (3): structure of compound (3a)

The IR spectrum analysis of compound (3e) showed two new absorption bands for the carbonyl group stretching at 1681 cm^{-1} and 1643 cm^{-1}. These bands correspond to the carbonyl group of acetophenone and the C=O group of the pyran ring. Following the formation of the Schiff base, the absence of the C=C bond absorption band associated with the pyran moiety facilitated a 1,4-conjugate addition (Michael addition) to the chromone system. This was followed by a rearrangement that resulted in the formation of compound through electron transfer to the imine bond C=CH-NH (3e).The spectra illustrated in Figure 8 and 9.

The analysis of the ^{1}H-NMR and ^{13}C-NMRin $DMSOd_6$ spectra indicated the formation of the expected product. The solvent molecule participated in the reaction pathway, and the process was carried out in ethanol at 30-35°C without the use of a catalyst. The ^{1}H -NMR spectrum in $DMSOd_6$ exhibited signals as a triplet and quartet at δ 1

ppm and δ 3.7 ppm, corresponding to CH_3 and CH_2 groups for the added ethoxy group. The appearance of the doublet at δ 11.9 ppm, attributed to NH, suggested that a 1,4-addition occurred at position 2 of the pyran ring base, with electron transfer occurring between the carbon atom of the pyran ring and the carbon atom of the azomethine (C═N) bond [14]**.** With good resolution, it is sometimes possible to observe splitting of the humps of N-H by the protons on adjacent carbon atoms.[15] Additionally, the ^{1}H-NMR spectrum displayed a multiplet signal with 9H at δ 7-8.26, which refers to the phenyl group, the benzene ring, and the C═CH group. The proton attached to this carbon was observed as a singlet at δ 6 ppm.

The structure of the expected product, as confirmed by the ^{13}C-NMR spectrum (Figures 4 and 10), displayed 14 lines in the aromatic region ranging from 100 to 156.11 ppm. The characteristic signals were found at δ 15.68, 27.40, 63.51 and100.52. ppm, which correspond to the CH_3, CH_3, CH_2, C-H, groups, respectively. Additional lines observed in the spectrum were attributed to the two carbonyl (C═O) groups of the acetophenone keto group and pyran, appearing at δ 198 ppm and δ 180.76 ppm. The signals belonging to aromatic region as δ 104 to156 indicated the presence of 13 C while the The ═CH observed at δ 140ppm.[14] Table (5 and 6)

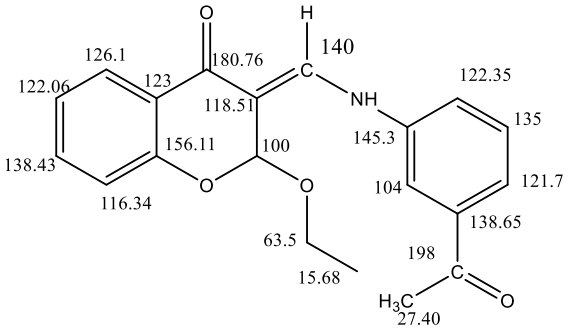
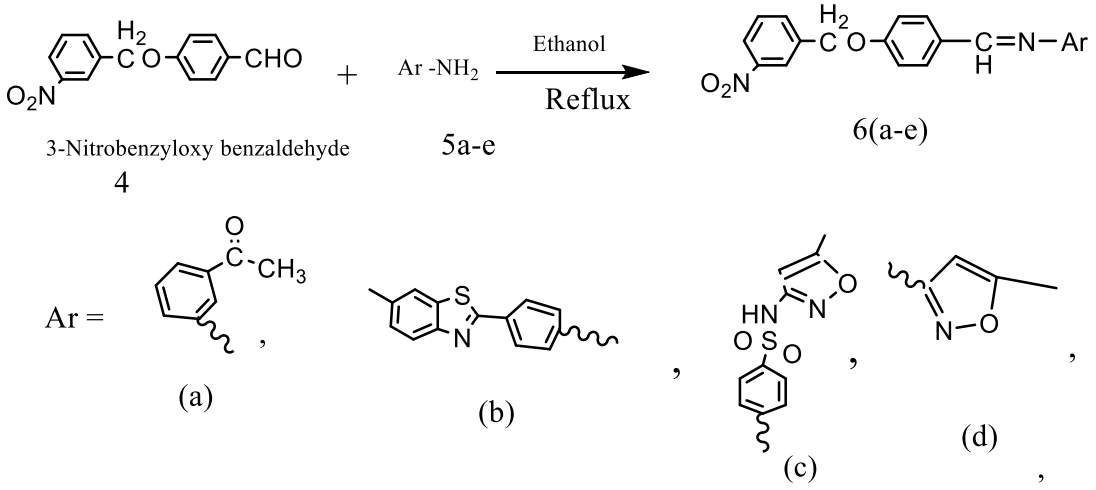


Figure (4): Structure of compound 3e

The second step of this work included the synthesis of Schiff bases derived from compound (4) through the condensation of some heterocyclic amines without addition of catalyst using reflux condition for 6 hours' scheme (2)



Scheme (2): The synthetic pathway of Schiff bases compounds (6a-e)

The structure of the products was confirmed using spectroscopic data (IR, ^{1}H-NMR, and ^{13}C-NMR). For instance, in the case of compounds 6a,6b,6d the disappearance of the NH_2 group and the appearance of peaks associated with the CH═N at 1600,1608,1604 cm^{-1}along with two absorption bands in the region of 1515-1527 cm^{-1} and 1342-1349 cm^{-1} for the asymmetric and symmetric stretching vibrations of the nitro group; additionally, a strong C—O—C absorption bands were noted at 1249-1257 cm^{-1} , and the disappearance of carbonyl group in the IR spectrum of Compound 4 at 1681.62cm-1 Figure (5,12,14).The ^{1}H-NMR spectrum of compound (6a) in $DMSOd_6$ Figure (13) indicated the formation of the product through the appearance of the three singlet signals at chemical shifts 2.64 ppm, 5.37 ppm, and 8.62 ppm, attributed to the CH_3, CH_2—O, and CH═N groups, respectively. [8]

The ^{13}C NMR analysis corroborated the findings from the IR and ^{1}H NMR spectral data, indicating the presence of 20 distinct lines. These lines correspond to the CH_3 at δ 27.37, the O-CH_2 at δ 68.58ppm, the C═NH at 161.22ppm, and the carbonyl group at 198.29ppm. The remaining lines are associated with three aromatic rings

(Ar), spanning from 115.63 to 166.43 for a total of 16 carbon atoms, as illustrated in Figure. (13). The ^{1}H-NMR spectrum of compound(6d)) showed the same signals at δ2.43ppm, 5.39ppm, ,6.49ppm and 8.36ppm related to appearance of CH_3,CH_2─O,CH,CH═N with displaying of 8H for two phenyl groups, Figure (15).^{13}C-NMR spectrum showed 16 lines for 16 carbon atoms corresponds to the carbons of the expected product , confirmed through the signals belongs to CH2-O carbons in all the synthesized compounds16 as illustrated in Figure (16) Table (5)

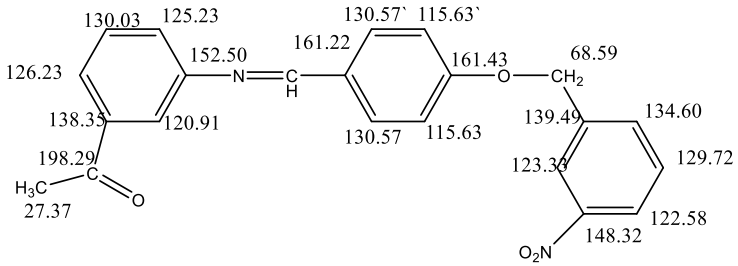


Figure (5); Structure of compound (6a)

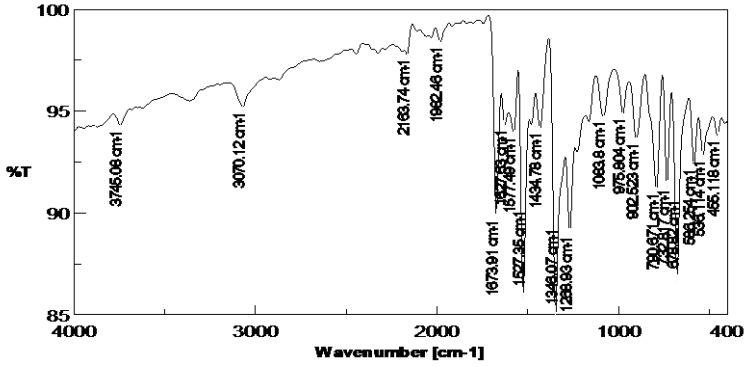
Antibacterial activity

The antibacterial activity was assessed against two type of bacterial strains: Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli.* This evaluation utilized the well diffusion method[11-13] at different concentrations, 1000 µg/ml, 500 µg/ml, and 250 µg/ml. The activity was qualitatively determined based on the presence and size of inhibition zones. Amikacin and ciprofloxacin served as positive controls.

The results indicated that the most effective compounds against *Staphylococcus aureus* were 3a, 3c, 3d, and 6c at the highest concentration of 1000 µg/ml. Compound 3d showed consistent activity (+++) at 1000 µg/ml, suggesting a strong antibacterial effect against *E. coli*. This effect is attributed to the substituted NO_2 group in the para position, which enhances binding affinity to the bacterial target, along with the hydrophilicity and lipophilicity of the overall compound influencing the bacterial cell wall (peptidoglycan).[17]Among the tested compounds, 3a, 3b, and 3c demonstrated moderate activity against *E. coli* at the concentrations of 250 µg/ml, , and 500 µg/ml and 1000 µg/ml, respectively. In contrast, compounds 3a and 3b exhibited weak activity against both bacterial strains. Compounds 6e were found to be inactive against both strains. Compound 6c showed moderate activity against *S. aureus* at the 1000 µg/ml whereas displayed excellent activity at a concentration of 1000 µg/ml against *E .coli.*

The antibacterial tests suggested that specific structural features of the compound 3 derivatives were more effective against Gram-positive bacteria compared to the series 6 compounds, likely due to better interaction with the thicker peptidoglycan layer of *S. aureus*.

The slightly improved efficacy of some compounds against *E. coli* indicates that certain modifications may enhance membrane penetration or interaction with Gram-negative bacterial targets. This may reflect an optimal balance between hydrophilic and hydrophobic regions that supports the antibacterial effect. Meanwhile, the standard drugs ciprofloxacin and amikacin produced significantly larger zones of inhibition.



Figure(6):IR spectrum of compound (3a)

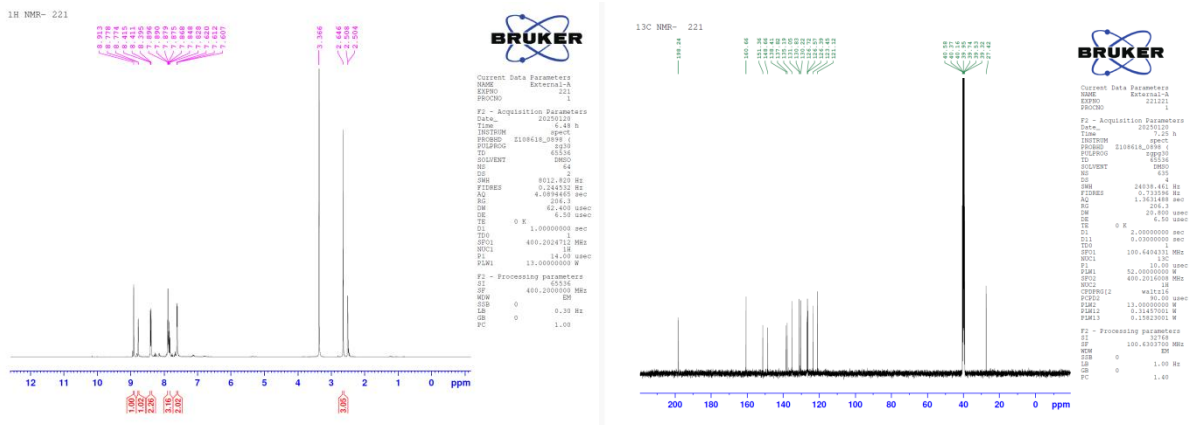


Figure (7): ^{1}H-NMR and ^{13}C-NMR spectra of compound (3a)

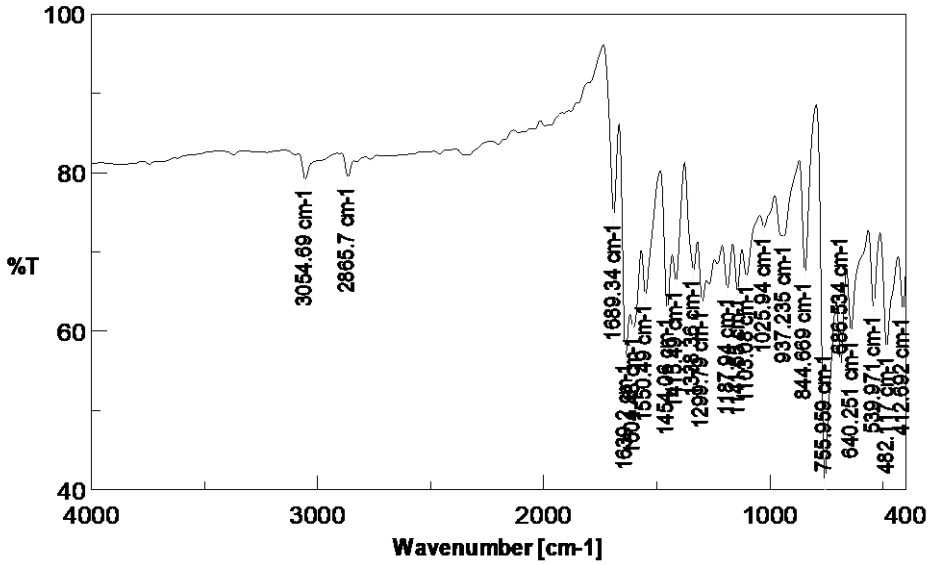


Figure (8): IR spectrum of 4-Oxo-4-*H*-1-Benzopyrane-3-carboaxldehyde

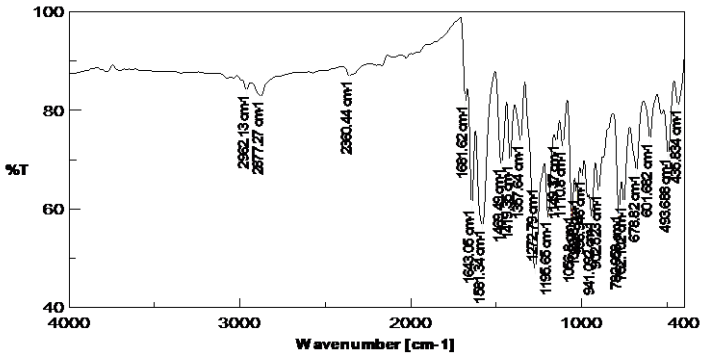
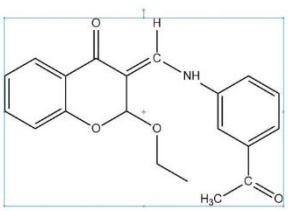


Figure (9): The IR spectrum of compound (3e)



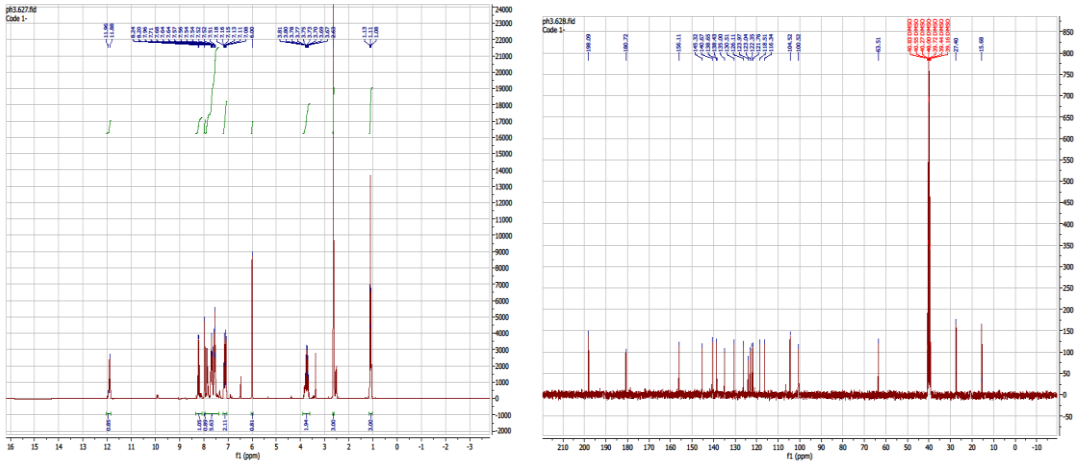
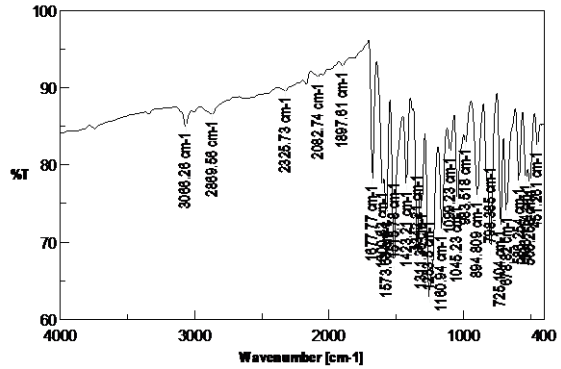
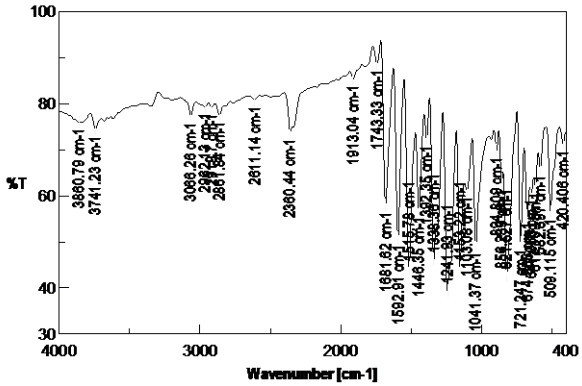


Figure (10): The ^{1}H-NMR spectrum ^{13}C-NMR spectra of compound 3e



Figure(11): IR Spectrum of compound 6a



Figure(12) IR spectrum of compound (4)

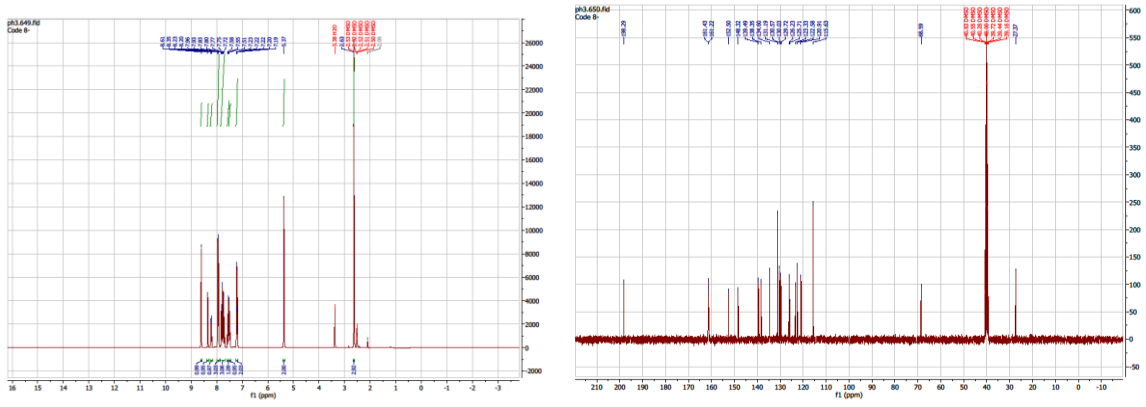


Figure (13): The ^{1}H-NMR and ^{13} C-NMR spectra of Compound (6a)

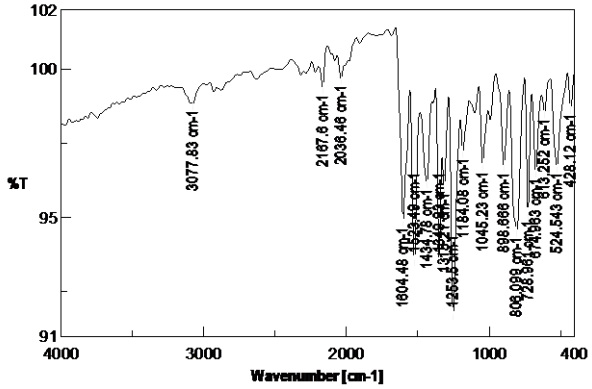


Figure (14): IR spectrum of compound (6d)

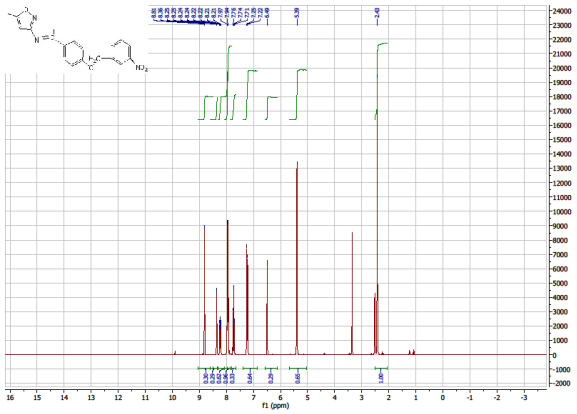


Figure (15): ^{1}H-NMR spectrum of compound(6d)

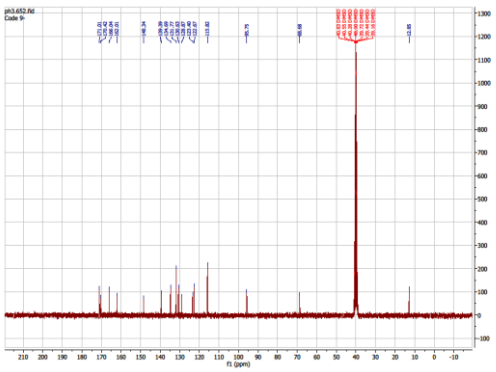


Figure (16): ^{13}C-NMR spectrum of (6d)

CONCLUSION

Two series of Schiff bases were prepared, specifically compounds 3a-e and 4a-e. The first step of this research study involved synthesizing Schiff bases derived from 3-aminoacetophenone. All synthesized compounds were obtained as powders, crystallized from suitable solvents, and yielded satisfactory results. The second step focused on synthesizing Schiff base compounds derived from3-NO2-Benzyloxybenzaldehyde. The successful synthesis of these Schiff bases, including both the 3-aminoacetophenone (1) derivatives and those derived from 3-nitrobenzyloxy benzaldehyde (4). The comprehensive preparation of compounds 3a-f and 6a-e demonstrates effective methodologies and underscores the robustness of the employed processes, as indicated by their satisfactory crystallization yields. This study not only contributes to the current collection of Schiff bases but also opens avenues for further exploration of their potential applications across various scientific fields. The insights gained from this research establish a solid foundation for future investigations into the properties and functionalities of these versatile compounds.

Among all tested compounds, 3d demonstrated the most promising antibacterial activity, particularly against E. coli, followed by 3c and 6c. The inactivity of compound 6e highlights the importance of specific structural features for antibacterial action. While none of the synthesized molecules matched the efficacy of ciprofloxacin, some displayed moderate activity worthy of further investigation and optimization.

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Competing interest: No competing of interests

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