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Synthesis, spectroscopic characterization and antibacterial activity of new series of Schiff base derived from 4-aminoantipyrine and 2-amino benzimidazole

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Abstract

Background and objective: Compounds having imine or azomethine (–C=N–) functional group are known as Schiff bases. Schiff bases compounds are found to be an active pharmacophore for the design and development of various bioactive lead compounds. In this study, several new Schiff base compounds have been synthesized and characterized.
Methods: Williamson ether synthesis process has been used to synthesize -alkyloxy and substituted benzyloxy of benzaldehyde. Differently substituted ether benzaldehydes used to react with 4-amino-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one in one hand and 1H-benzo[d]imidazol-2-amine on the other hand to produce Schiff base compounds.
Results: Synthesized ether derivative compounds (**3**a-e) were converted to new series of Schiff bases (**4**a-e and **5**a-e) by condensation of equal molar amounts of compounds (**3**a-e) with different heterocyclic amines dissolved in absolute ethanol. All synthesized compounds were confirmed by (IR, ^{1}H-NMR, and ^{13}CNMR) spectroscopy. All synthesized compounds were evaluated for antibacterial activities in vitro against Gram-positive and Gram-negative bacteria.
Conclusion: All compounds were purely synthesized, and all compounds were indicated growth inhibition against Escherichia coli, and Staphylococcus aureus, respectively with different inhibition zones staring from 13 to 33 mm.
Keywords: Schiff base; Williamson ether synthesis; Biological activity; Azomethine.

Introduction

Heterocyclic compounds containing one or more hetero atoms having the range of applications in our life, such as used as pharmaceuticals, agrochemicals, and veterinary products.[1,2] Schiff bases play a major role in their significant bio-activities and containing azomethine (-N=CH-) as an active pharmacophore.[3] Schiff bases considered as important starting materials to synthesis new drug design and intermediate in organic syntheses, or rubber additives.[4] They have received much attention in the field of chemistry and biology due to their chemotherapeutic value.[5] Schiff bases are formed by the reaction between primary amine with an aldehyde or a ketone under specific conditions and used as amino protective groups in organic synthesis.[6-8] Metal ions can form complex with Schiff bases as a ligand and liquid crystals in analytical, medicinal, and polymer chemistry.[9,10] Based on the wide spectrum of biological profile of Schiff bases and heterocyclic compounds and their importance in pharmaceutical and biological fields, it was thought of interest to accommodate imidazole and pyrazolone moieties with alkyloxy and substituted benzyloxy group and azomethine bond in a single molecular framework to synthesis of new series of Schiff bases (Imines) of heterocyclic amine compounds for enhancing biological activity. This study aimed to synthesize several 4- hydroxyl benzaldehyde derivatives by a substitution reaction with different alkyl halide followed

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by synthesis of series of new active pharmacophore Schiff base compounds (**4**a-e) and (**5**a-e) derived from 4-aminoantipyrine and 2-minobenzimidazole with substituted benzaldehyde containing substituted benzyloxy and alkyloxy group in para position by a condensation reaction. The biological activity of the synthesized compounds studied on some of the gram-positive bacteria and gram-negative bacteria. Antipyrine (1,5-dimethyl-2-phenylpyrazole-3-one) is a compound that possesses a pyrazolone moiety with a five-membered lactam ring containing two nitrogen and a ketone in the same molecule. Antipyrine and its 4-amino derivative (4-amino-1,5-dimethyl-2-phenylpyrazole-3-one) have shown outstanding pharmacological properties such as anti-inflammatory, analgesic, antiviral, antipyretic, antirheumatic, and biological activity.[11,12] Benzimidazole was the second heterocyclic compound used for organic synthesis and preparing a wide variety of substituted benzimidazoles and application of such compounds in the development of new chemotherapeutic agents are investigated.[12] This study aimed to synthesize and characterize several new Schiff base compounds and to screen their antibacterial activity.

Methods

This experimental study was done at a College of Pharmacy, Hawler Medical University, from 20th of February to 25th of April 2018 starting from different derivatives of alkyl halides, phenol, and amines. Melting points were recorded using a Stuart scientific Melting Point (Table 1). Infrared spectra were recorded in the range 4000-600 cm-1 using a Shimadzu Scientific Instruments' IR, as KBr disc (Chemistry Department, College of Education, Salahadden University, Erbil. Samples were either thin films or powders. All absorptions are quoted in cm^{-1}. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Brukeravance (600 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetra-methylsilane as an internal standard. NMR spectra were recorded in solutions in deuterated-dimethylsulfoxide (DMSO-d_6).

Table 1: Some physical constants of synthesized compounds.

Compds	Chemical formula	M.P	Yield	Color	Comp.	R-	M.P	Yield %	color
4a	$C_{25}H_{23}N_3O_2$	146-148	90	Light yellow	3a	$C_6H_4CH_2O$-	63-65	93	white
4b	$C_{25}H_{22}N_4O_4$	167-170	92	yellow	3b	3-NO_2-$C_6H_4CH_2O$-	53-59	87	yellow
4c	$C_{22}H_{25}N_3O_2$	155-157	80	Light yellow	3c	C_4H_{10} O-	253	85	Yellow liquid
4d	$C_{26}H_{22}BrN_3O_3$	176-178	85	Brown	3d	4-Br-$C_6H_5COCH_2O$-	96-98	90	Light brown
4e	$C_{25}H_{22}ClN_3O_2$	138-139	83	white	3e	3-$ClC_6H_6CH_2O$-	53-55	85	white
5a	$C_{21}H_{17}N_3O$	210-212	85	Light brown					
5b	$C_{21}H_{16}N_4O_3$	232-234	85	yellow					
5c	$C_{18}H_{19}N_3O$	239-241	75	Light yellow					
5d	$C_{22}H_{16}BrN_3O_2$	243-245	80	brown					
5e	$C_{21}H_{16}ClN_3O$	225-227	75	Light yellow					

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Results

Synthesis of 4-AlkoxyBenzaldehydes (3a-e)[4]

A mixture of 4-hydroxybenzaldehyde (0.05mole) and K_2CO_3 (0.11 mole) was dissolved in10 ml of absolute ethanol and stirred at room temperature for 2 hours. 0.05 mole of alkyl halides were added to the mixture and heated under reflux for 7 hours. The mixture was powered into ice and filtered. Products were recrystallized from the suitable solvent (Table 2 and 3).

Synthesis of (phenylpyrazolonelidene) 4 –substitutedphenyl (4a-e)[4]

4-aminoantipyrine(2.21 g, 0.01mole) was dissolved in 10 ml of absolute ethanol, appropriate aldehyde (0.01 mole) was added to the mixture. The reaction mixture was refluxed for 5 hours and then cooled. The products were precipitated and filtered off, recrystallized from absolute ethanol. All physical properties are listed in Table1 and 2.

Synthesis of benzimidazolidene - 2-substituted phenyl[4]

2-aminobenzimidazole(1.33 g, 0.01mole) was dissolved in 10 ml of absolute ethanol; appropriate aldehyde (0.01 mole) was added to the mixture. The reaction mixture was refluxed for 5 hours and then cooled. The products were precipitated and filtered off and recrystallized from absolute ethanol. The physical properties are listed in Table 1 and 2.

Table 2: Infrared spectral data in cm^{-1} for synthesized compounds.

Comp.	C=O	NH	CH Ar-H	CH_2 R-H	C-H Imine	C-O Ether	N=C
4a	1637		3034	2941	2883	1238	1602
4b	1647		3099 3076	2935	2887	1242	1608
4c	1645		3055	2958 2931 2904	2872	1242	1597
4d	1654 1701		3061	2922	2850	1226	1654
4e	1647		370	2928	2872	1236	1608
5a		3350	3057	2829	2744	1261	1687 1600
5b		3300	3070	2952	2860	1247	1685 1604
5c		3300	3086	2958	2873	1246	1685 16o4
5d		3350	3066	2972	2875	1217	1693 1598
5e		3230	3091	2879	2790	1220	1685 1602

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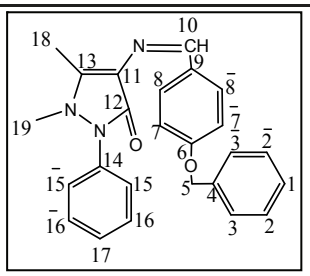
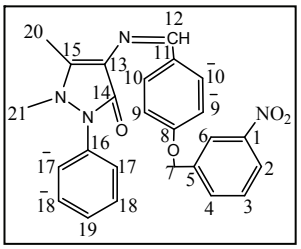
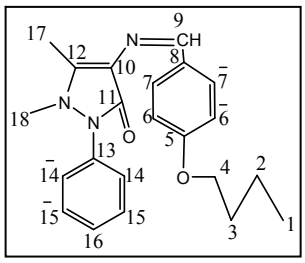
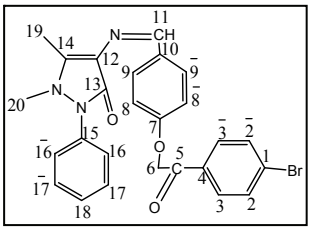
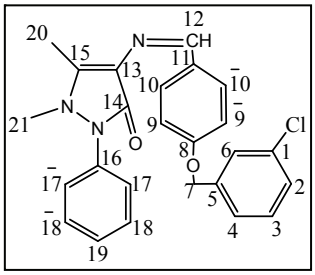
Table 3: ^{1}H-NMR and ^{13}C-NMRchemical shift assignment in ppm for synthesized compounds

Compounds	^{1}H-NMR and ^{13}C-NMR Chemical shifts in ppm
4a 	^{1}H NMR (600 MHz, DMSO-d_6) δ 9.52 (s,1H, CH=CN), 7.34-7.77 (m, 14H,Ar-H), 5.17 (s, 2H, CH_2), 3.17(s, 3H, NCH_3), 2.43(s, 3H, CH_3), ^{13}C NMR (151 MHz, DMSO) δ 160.58 (C_{10}), 160.29 (C_{12}), 154.69(C_6), 152.34 (C_{13}), 137.27 (C_4), 135.16 (C_{14}), 131.01(C_9), 129.57 ($C_{8,8}^{-}$), 129.33 ($C_{16,16}^{-}$), 128.93 ($C_{2,2}$), 128.38 (C_1), 128.18 ($C_{3,3}^{-}$), 127.18 (C_{17}), 124.83 ($C_{7,7}^{-}$), 117.41 ($C_{15,15}^{-}$), 115.51 (C_{11}), 69.84 (C_5), 36.00 (C_{19}), 10.25 (C_{18}).
4b 	^{1}H NMR (600 MHz, DMSO-d_6) δ 9.52 (s, 1H, CH=CN), 7.13-8.34 (m, 13H,Ar-H), 5.34 (s, 2H, CH_2), 3.15 (s, 3H,NCH_3), 2.44 (s, 3H, CH_3). ^{13}C NMR (151 MHz, DMSO) δ 160.25 (C_{12}), 160.14 (C14), 154.56 (C_8), 148.34 (C_{15}), 139.70 (C_1), 135.14 (C_5), 134.64 (C_{16}) 131.41(C_4), 130.58 ($C_{10,10}^{-}$), 129.58 ($C_{18,18}^{-}$), 129.38 ($C_{3,11}$), 127.21 (C_{19}), 124.86 ($C_{2,6}$), 123.28 ($C_{17,17}^{-}$), 117.41 ($C_{9,9}$), 115.51 (C_{13}), 69.53 (C_7), 35.98 (C_{21}), 10.25 (C_{20}).
4c 	^{1}H NMR (600 MHz, DMSO-d_6): δ 9.52 (s, 1H, CH=CN), 7.0 – 7.8 (m, 9H, Ar-H), 4.02 (t, 2H, CH_2), 3.14 (s, 3H, NCH_3), 2.43 (s, 3H, CH_3), 1.74 – 1.68 (m, 2H, CH_2), 1.44 (h, 2H, CH_2), 0.94 (t, 3H, CH_3). ^{13}C NMR (151 MHz, DMSO): δ 160.95) C_9), 160.31) C_{11}), 154.82)C_5), 152.33) C_{12}), 135.18) C_{13}), 130)66.C_8), 129.56) $C_{7,7}^{-}$), 129.34) $C_{15,15}^{-}$), 127) 15.C_{16}), 124.83($C_{14,14}^{-}$), 117.30($C_{6,6}^{-}$), 115.51 (C_{10}), 67.74 (C_4), 36.02 (C_{18}), 31.16 (C_3), 19.19 (C_2), 14.16 (C_1), 10.25 (C_{17}).
4d 	^{1}H NMR (600 MHz, DMSO-d_6): δ 9.53 (s,1H, CH=CN), 7.10- 7.77 (d, 13H, Ar-H), 5.19 (s, 2H, CH_2), 3.34 (s, 3H, NCH_3), 3.15 (s, 3H, CH_3). ^{13}C NMR (151 MHz, DMSO): δ 191 (C_5), δ 160.29(C_{11}), 160.26 (C_{13}), 154.62 (C_7), 152.38 (C_{14}), 139.88 (C_{15}), 135.15 (C_4), 133.60 ($C_{2,2}^{-}$), 131.20 ($C_{3,3}^{-}$), 130.87 ($C_{9,9}^{-}$), 129.58 ($C_{17,17}^{-}$), 129.35 (C_1), 128.30 (C_{10}), 127.83(C_{18}), 127.19 ($C_{8,8}^{-}$), 126.70 ($C_{16,16}^{-}$), 115.52 (C_{12}), 68.88 (C_6), 35.99 (C_{20}), 10.25 (C_{19}).
4e 	^{1}H NMR (600 MHz, DMSO-d_6) δ 9.50 (s, 1H, CH=CN), 7.1-7.8 (m, 13H, Ar-H), 5.54 (m, 2H, CH2), 3.16 (s, 3H, NCH_3), 2.09 (s, 3H, CH_3). ^{13}C NMR (151 MHz, DMSO): δ 164.57 (C_{12}), 160.11 (C_{14}), 152.57 (C_8), 152.46 (C_{15}), 151.86 (C_5), 148.50 (C_{16}), 135.31 (C_1) 132.64(C_3), 131.68 ($C_{10,10}^{-}$), 130.45 ($C_{18,18}^{-}$), 129.56 ($C_{2,6}$), 126.30 (C_{11}), 124.84(C_4), 123.05(C_{19}), 122.95 ($C_{9,9}^{-}$), 119.74($C_{17,17}^{-}$), 116.19 (C_{13}), 56.85 (C_7), 35.96 (C_{21}), 10.21 (C_{20}).

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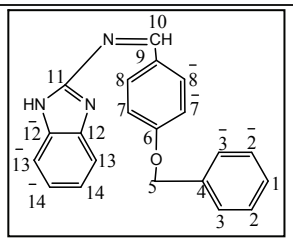
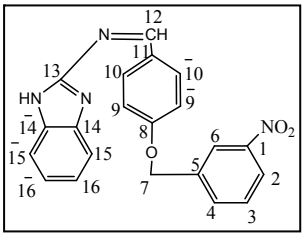
5a



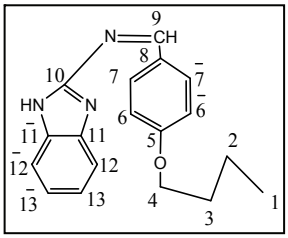
^{1}H NMR (600 MHz, DMSO-d_6): δ 9.88 (s, 1H, CH=CN), 7.22-7.89 (m, 13H, Ar-H), 5.24 (s, 2H, CH_2),7.21 (s, NH) ^{13}C NMR (151 MHz, DMSO) δ 191.87(C_6), 163.79(C_{10}), 163.59(C_{11}) 136.49(C_4), 132.26 ($C_{12,12}^{-}$), 130.25 ($C_{2,2}^{-}$,$_{8,8}^{-}$), 128.98($C_{1,9,3,3}^{-}$), 128.54 ($C_{14,14}^{-}$), 128.32($C_{13,13}^{-}$), 115.75($C_{7,7}^{-}$), 70.13 (C_5).

5b



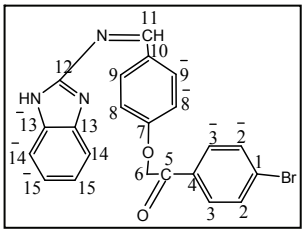
^{1}H NMR (600 MHz, DMSO-d_6): δ 8. 89 (s, 1H, CH=CN), 7.23-8,37 (m, 12H, Ar-H), 5.8 (s, 1H, NH), 5.42 (s, 2H, CH_2). ^{13}C NMR (151 MHz, DMSO): δ 184.10(C_8), 165.44(C_{12}), 148.36(C_{13}),140.20(C_1),134.95(C_5),134.71($C_{14,14}^{-}$),134.49(C_4), 132.55($C_{10,10}^{-}$),130.81 (C_3), 130.64 (C_{11}), 123.43 (C_6), 123.01 ($C_{16,16}^{-}$), 122.75 (C_2), 119.75 ($C_{15,15}^{-}$), 115.97($C_{9,9}^{-}$),68.76 (C_7).

5c



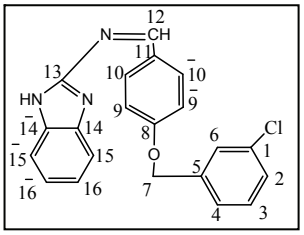
^{1}H NMR (600 MHz, DMSO-d_6): δ 9.80 (s, 1H, CH=CN), δ 6.9- 7.9 (m, 8H,Ar-H) ,4.02 (t,2H, CH_2), 1.73 – 1.68 (m, 2H, CH_2), 1.44 (q, 2H, CH_2), 0.93 (t,3H, CH_3), 6.7 (s, NH). ^{13}C NMR (151 MHz, DMSO): δ 168.47(C_9), δ 162.40(C_5), 155.30 (C_{10}), 138.25($C_{11,11}^{-}$), 131.70 ($C_{7,7}^{-}$), 125.04 (C_8), 120.04 ($C_{13,13}^{-}$), 114.48($_{12,12}^{-}$) ,111.87($C_{6,6}^{-}$,) 67.87 (C_4), 31.09 (C_3), 19.16 (C_2), 14.13 (C_1).

5d



^{1}H NMR (600 MHz, DMSO-d_6) δ 9.86 (s, 1H, CH=CN), 6.84- 7.90 (m, 12H, Ar-H), 5.20 (s, 1H, CH_2) 7.10 (s, NH). ^{13}C NMR (151 MHz, DMSO) δ 189 (C_5), δ 168.47(C_7), δ 162.01(C_{11}), 155.66 (C_{12}), 139.63 ($C_{13,13}^{-}$), 133.60 (C_4), 131.80 ($C_{2,2}^{-}$,$_{3,3}^{-}$), 130.90 ($C_{9,9}^{-}$), 128.37 (C_{10}), 128.88 (C_1), 126.75 ($C_{15,15}^{-}$), 119.45 ($C_{14,14}^{-}$), 115.04($C_{8,8}^{-}$), 68.94 (C_6).

5e



^{1}H NMR (600 MHz, DMSO-d_6): δ 9.87 (s, 1H, CH=CN), 6.25 – 8.23 (m, 12H, Ar-H), 5.62 (s, 2H, CH_2) 6.17 (s, NH). ^{13}C NMR (151 MHz, DMSO): δ 191.62 (C_8), 186.93 (C_{12}), 175.40 (C_{13}), 136.10 (C_5), 132.38 ($C_{14,14}^{-}$) 132.29 (C_1), 132.14 (C_3), 131.48 ($C_{2,6}$), 130.34 ($C_{10,10}^{-}$), 129.49 (C_{11}), 125.75 (C_4), 124.86 ($C_{16,16}^{-}$), 116.66 ($C_{15,15}^{-}$), 115.49 ($C_{9,9}^{-}$), 70.50 (C_7).

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Biological Activity

Mueller-Hinton agar medium was used to study the antibacterial activity of the synthesized compounds (2-5) against Escherichia coli and Staphylococcus aureus. 0.0512g of each test compound was dissolved in 10 ml of 20 % of DMSO. Two different concentrations were prepared by using half of the prepared solution with 5 ml of 20 % DMSO with 256 and 512µg/ml including another concentration to prepared by 5 ml of 20 % DMSO 128µg/ml. Sterile cork borer (6mm) was used to prepare cups constructed in Petri plates, and 0.1 ml of each tested compound was added separately into each well, and then bacterial plates were incubated at 37 C in 24 hrs. The Zone of inhibition fashioned by each compound was measured in mm (Table 4).

Discussion

The first stage of this work involves the synthesis of ether derivatives forbenzaldehyde(**3**a-e) from *p* -hydroxyl benzaldehyde using the Williamson ether synthesis method.[13] The reaction proceeded under reflux condition using potassium carbonate, and the nucleophilic substitution reactions were progressed smoothly, and products were obtained in very good yields, and high purity for the alkyloxy and substituted benzylxoybenzaldehyde. All synthesized compounds were studied by NMR and IR spectroscopy. IR spectra for all ether compounds showed the disappearance of OH band for p-hydroxyl benzaldehyde as a starting material that appeared at (3400 cm^{-1}), whereas, new bands at (1217-1352 cm^{-1}) were shown due to the new C-O

Table 4: Diameter of inhibited zones in millimeters as a measure of antibacterial activity of the synthesized compounds (**4a-e** and **5a-e**) and some standard drugs.

Compounds		*Escherichia coli*		*Staphylococcus aureus*	
		256 µg	512 µg	256 µg	512 µg
4	**A**	**-**	32	-	-
	B	**-**	24	-	-
	C	**-**	-	-	28
	D	**-**	14	-	-
	E	**-**	-	-	27
5	**A**	**-**	18	-	-
	B	**-**	20	-	13
	C	**-**	-	-	33
	D	**-**	22	-	-
	E	**-**	25	-	19
Amikacin		19–26		20–26	
Cefalotin		15–21		29–37	
Tetracycline		18–25		24–30	
Chloramphenicol		21–27		19–26	
Nalidixic acid		22–28		-	
Vancomycin		**-**		17–21	

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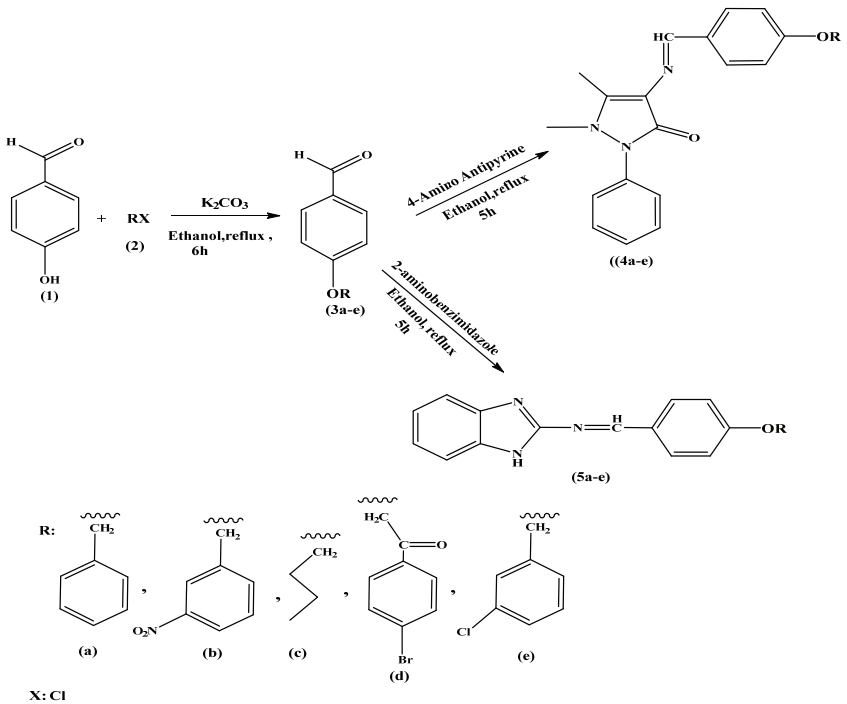
bond vibration indicated the formation of the desired ether compounds (*vide infra*) (Table 2). Ether derivatives of substituted benzaldehyde compounds (**3**a-e) have been synthesized successfully by using the previous conditions reacting with an appropriate amine in the presence of K_2CO_3 as a catalyst (Scheme 1).[14] Substituted alkoxy and substituted benzyloxybenzaldehyde benzaldehyde were used as starting materials to react with 4-amino-antipyrineto prepare new series of Schiff bases (imines) using condensation method without the catalyst. All synthesized compounds were elucidated by IR and NMR spectroscopy. Synthesized compounds were washed with water to remove hydrophilic starting materials, and hexane has been used to remove trace amount of lipophilic materials. IR, ^{1}H- and ^{13}C-NMR spectral data for synthesized compounds were consistent with expected structures. The Infrared spectra for the synthesized imines compounds showed the disappearance of the vibration frequency of C=O groups at (1710) $cm^{-1}$of C=O group for substituted of benzaldehyde and appearance of a new band for azomethines bond (–N=CH-) in the region between (1597-1654) Cm^{-1} (Table 2). The bands at 3431 and 3400 cm^{-1} for 4-amino antipyrine are assigned to N-H asymmetric and symmetric stretching vibrations disappeared in the IR spectrum of Schiff bases, the C=Ostretching vibration of pyrazolone ring observed at 1637-1654cm^{-1} in the IR spectra of the synthesized compounds. Carbonyl bands are the most characteristics bands in Infrared spectra. The substituted benzene gives rise to C-H stretching, C-H out-of-plane bending and C-H in-plane bendings. The bands around 3000 - 3100 cm^{-l} are assigned to-H stretching vibrations. The appearance of a singlet signal peak at δ (8-10) ppm showed azomethin protons (-N=CH) in ^{1}HNMR and significant peaks were distinguishable for substituted benzaldehyde for all synthesized compounds. Compound **4a** is selected as a representative of their series for the study of ^{1}H-NMR, singlet signal atδ (9.5) ppm with a single signal for (CH_2O) group at δ 5.2 ppm indicates the presence of



Scheme 1: Schiff base synthetic compound's pathway.

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benzyloxy($C_6H_5CH_2O$-) group in the structure of a new compound and the multiplet signals from δ 7.2-7.7 ppm for 14 protons of two phenyl rings. The two methyl groups (CH_3) for pyrazolone moiety observed at δ 2.44 (CH_3) ppm and δ 3.1 (NCH_3) (Figure 1 and Table 3).

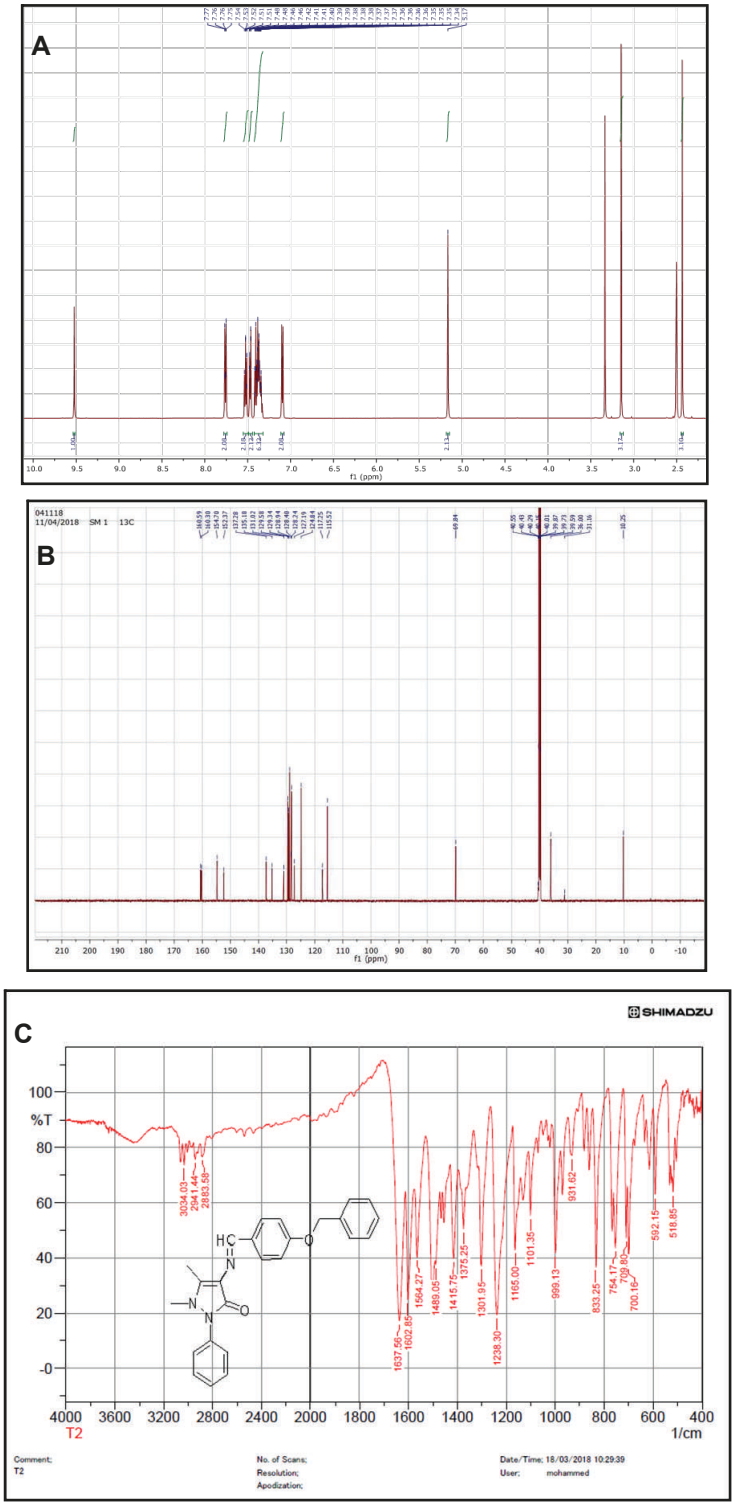

Figure 1: (A) ^{1}H-NMR, (B) ^{13}C-NMR, and (C) IR spectra of compound **4**a.

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Further verification for the formation of new Schiff bases was attained from ^{13}C-NMR spectra (Table 3); with the signal at(68-70) ppm due to the carbon atom that attached to oxygen atom CH_2O group confirms the substitution reaction on hydroxyl group. The depicted signals in the aromatic region for the different type of carbons at different chemical shifts were inconvenient with a number of carbon atom in each compound with the observation of lines at δ (160-186) ppm related to azomethines carbon (-N=CH) (*vide supra*). The spectra of compounds (**4**a-e) also revealed several absorption bands related to the reacted 4-aminoantipyrineat δ 10 ppm,35 ppm and δ 152-160 ppm attributed to the two methyl group- and carbonyl group (C=O) of pyrazolone moiety (Table 3). The aromatic carbon for compounds(**5**a-e) showed different type of carbons in different chemical shift at δ 164-115 ppm,^{13}C-NMR data for compound **5**c provided confirmatory evidence for substitution reaction on hydroxyl group exhibited four lines at 14, 19,31,68 ppm, respectively for butoxy group $CH_3CH_2CH_2CH_2O$- supported the formation of Schiff base via azomethines carbon (-N=CH) resonance at 168 ppm (Table 3 and Figure 2).

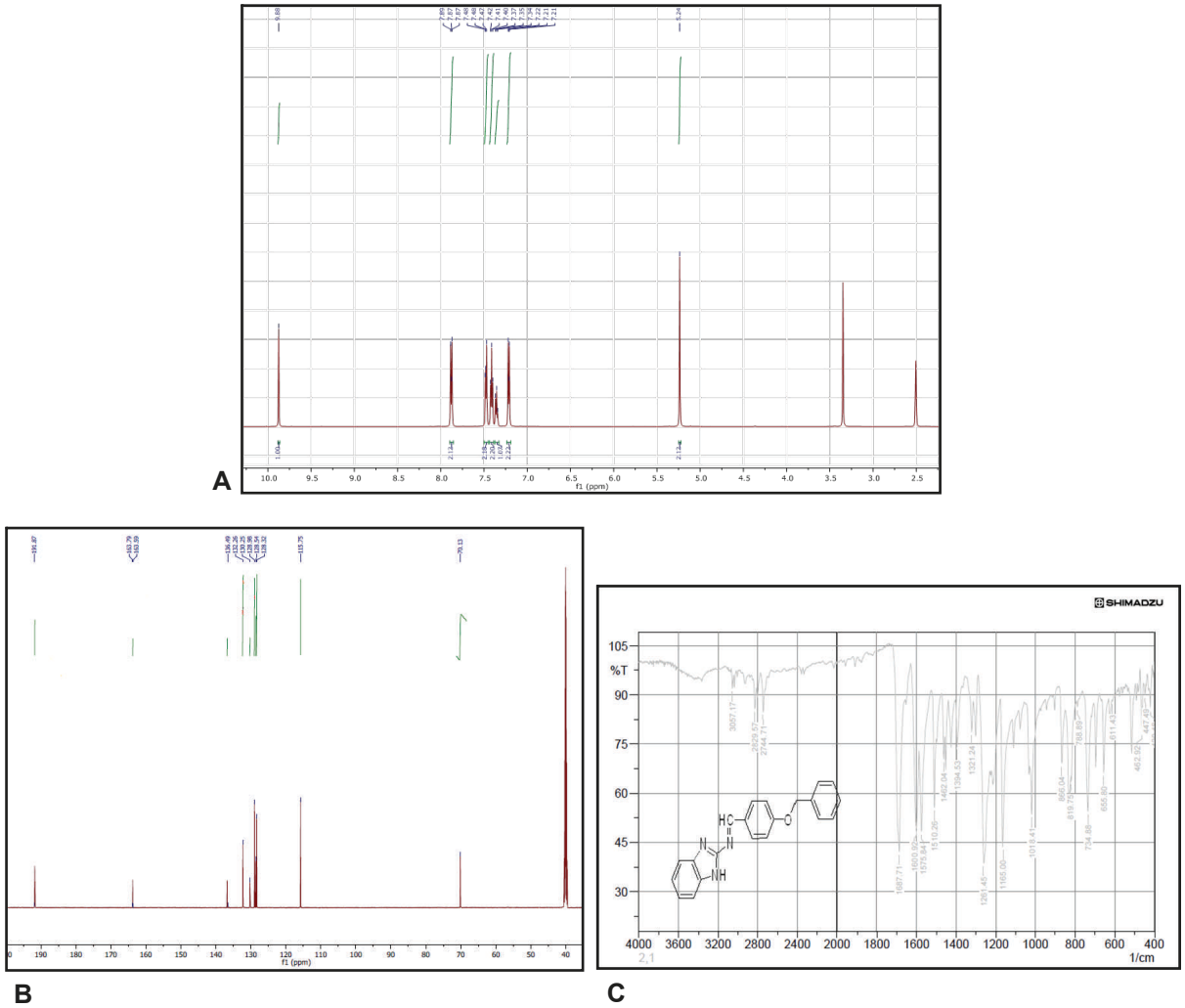

Figure 2: (A) ^{1}H-NMR, (B) ^{13}C-NMR, and (C) IRspectra of compound **5**a.

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Biological activity

The biological activity of the present compounds in terms of the anti-bacterial property was analyzed against two well known pathogenic gram-negative and gram -positive organisms such as Escherichia coli, and Staphylococcus aureus, respectively. The activity was tested after the dissolution of all the compounds **4**, **5** (a-e) in DMSO, which was used as a negative control in the experiment. The results of the bacterial growth inhibition are shown in Table 4 (vide *supra*) along with the corresponding positive and negative controls. All synthesized compounds except **4c**, **4e**, and **5c** showed significant growth inhibition (14–32 mm) against Escherichia coli, indicating that the experimental set and procedures are appropriate for the test. The most active compound against escherichia coli was compound 4a with 32 mm zone. Whereas, compound **4b**, **4e,** and **5c** indicated anti-distinguishable inhibition zone against Staphylococcus aureus organism with an inhibition zone of 13–33 mm. With this exception, compounds **5b,** and **5e** showed inhibition zone against both Escherichia coli, and Staphylococcus aureus with inhibition zones of 20, 25, and 13, 19 mm, respectively (Table 4).

Conclusion

In the present work, several substituted Schiff bases have been synthesized via using substituted 4-alkyloxy and substituted benzyloxybenzaldehyde aldehydes that prepared by hydroxyl benzaldehyde with different alkyl and substituted benzyl halide. The 4-alkyloxy andaldehydes were used as starting material to react with the different substituted amine to produce successfully several Schiff base compounds. 4-amino-1,5-dimethyl-2-phenyl -1,2-dihydro-3H-pyrazol-3-one was used to react with substituted 4-alkyloxy and aryloxyaldehydes to produce pure Schiff base compounds (**4**a-e). 1H-benzo[d] imidazol-2-amine was also used to react with substituted 4-alkyloxy substituted beznyloxy benzaldehyde in high purity without using chromatography techniques, and using sometimes hexane to purify products. All synthesized compounds were screened in biological activity indicated significant growth inhibition against Escherichia coli, and Staphylococcus aureus, respectively with different inhibition zones staring from 13 to 33 mm.

Competing interests

The authors declare that they have no competing interests.

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