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Synthesis and Spectroscopic Characterization of Some New Biological Active Azo–Pyrazoline Derivatives

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Abstract A number of 3-[4-(benzyloxy)-3-(2-Chlorophenylazo)-phenyl]-5-(substituted-phenyl)-1- substituted-2-pyrazolines(4a-j) and (5a-j) have been synthesized by diazotization of 2-chloroaniline and its coupling reaction with 4-hydroxy acetophenone, followed by benzyloxation of the hydroxyl group to give the substrate [4-benzyloxy-3-(2-chlorophenylazo)-acetophenone (1)].The prepared starting material (1) has been reacted with different substituted benzaldehydes to give a new series of chalcone derivatives 1-[(4- benzyloxy)-3-(2-chloro-phenylazo) -phenyl]-3-(substituted phenyl)-2-propen-1-one (3a-j) , in high yields and in a few minutes, and the later compounds were treated with hydrazine hydrate according to Michael addition reaction to afford a new biolological active target compounds (4a-j) and (5a-j). Furthermore, The structures of the newly synthesized compounds were confirmed by FT-IR, ^{13}C-NMR,^{13}C-DEPT &^{1}H-NMR spectral data. The chalcone and pyrazoline derivatives were evaluated for their anti bacterial activity against *Escherichia coli* as gram negative and *Staphylococcus aureus* as gram positive, the results showed significant activity against both types of bacteria.

Keywords : diazotization , benzyloxation ,Chalcone , Pyrazoline, Anti-bacterial activity.

Introduction

Azo-coupling is one of the most important reactions for combining aromatic rings [1]and preparing azobenzene derivatives containing active functional groups as a precursor for further synthesis to give different organic molecules such as : azo-amide[2] , azo-imine [3] and azo- chalcone [4]. Azo compounds are important as synthetic dyes[5,6] and cosmetics [7]. Chalcones and azo-chalcones are useful precursor for the synthesis of different heterocyclic compounds like pyrimidines [8], thiazepines [9] and Pyrazolines[10,12]. All derivatives are known to possess impressive biological activities. Such as: anti-malarial [13], anti-bacterial [14] , anti-oxidative[15] , anti-fungal [16], anti-leishmanial [17], anti- tumour

[18], central nervous system [19], anti-histaminic [20]. Herein , we have described the synthesis of some new azo-pyrazoline compounds derived from 2-chloro aniline and p-hydroxy acetophenone with evaluation their anti bacterial studies.

Experimental

Melting points were determined using an Electrothermal melting point apparatus , IR spectra were recorded on a Bio-rad Merlin FT-IR spectroscopy Mod FTS 3000, using KBr disc. ^{1}H-NMR and C^{13}-NMR and ^{13}C-DEPT-135 spectra were recorded on a Bruker(300MHz) with TMS as internal reference in(Jordon) :

1-Preparation of 3-(2-chlorophenylazo)-4-hydroxyacetophenone (1)[21]

The pure compound prepared according to the procedure[21] as yellow crystals, of 3-(2-chlorophenyl-azo)-4-hydroxyacetophenone (1). ($C_{14}H_{11}ClO_2N_2$), m.p. (148-150C^{o}), yield of (10.86gm, 99%). IR (cm^{-1})str. 3431 (OH), 1679 (C=O), 1607 (C=C), 1557 (-N=N-), 1276 (C-O), ^{1}H-NMR (ppm): 2.68 (s , 3H , H_1-CH_3);; 7.12 (d , 1H , $H_{5'}$) ; 7.41(d , 1H , H_{11}) ; 7.49 (d , 1H , H_{12}) ; 7.63 (d , 1H , H_{13}) ; 7.98 (d , 1H , H_{10}) ; 8.06 (d , 1H , H_4) ; 8.64 (s , 1H , H_8) 12.25 (s , 1H , OH).

2-Preparation of 3-(2-chlorophenylazo)-4-benzyloxyacetophen-one (2) [22]

A mixture of 3-(2-chlorophenylazo)-4-hydroxy acetophenone (15gm, 0.0546 mol), benzyl bromide (14.02gm, 0.082 mol) and anhydrous K_2CO_3 (15.1gm, 0.109 mol) in ethanol (200 ml - 96%) was refluxed with stirring for 6hrs. The cooled solution poured into water, solid materials immediately was obtained. The product was filtered off, washed several times with cold water, dried and recrystallized with a mixture (1:2) xylene: ethanol to obtain yellow-orange crystals of 3-(2-chlorophenylazo)- 4-benzyloxy acetophenone (2). ($C_{21}H_{17}ClO_2N_2$), m.p. (133-134C^{o}), yield (11.9 gm, 59%). IR (cm^{-1}) str, 1673 (C=O), 1598 (C=C), 1532 (-N=N-), 1271 (C-O), ^{1}H-NMR (ppm) :2.61 (s , 3H , H_1-CH_3); 5.39 (s , 2H , H_{15}) ; 7.16 (d , 1H , H_5) 7.35-7.51 (m , 5H , $H_{17, 18, 19, 20, 21}$) ; 7.62 (d , 1H , H_{11}) ; 7.71 (d , 1H , H_{12}) ; 7.82 (d , 1H , H_{13}) ; 7.91 (d , 1H , H_{10}) ; 8.04 (d , 1H , H_4) ; 8.45 (s , 1H , H_8). ^{13}C-NMR : C_1: 26.38 ; C_{15}: 71.28 ; C_5: 116.91 ; C_8 : 119.06 ; $C_{10,}$: 126.13 ; C_{11}:127.90 ; $C_{17,21}$:128.48 ; C_{14}:129.22; C_{19}: 129.59; $C_{18, 20}$: 130.48 ; C_{13}: 131.08; C_{12}:131.52 ; C_3: 132.83; C_4: 133.49; C_7: 135.39; C_{16}: 136.13; C_9: 142.14; C_6:159.84; C_2: 196.7. Dept-135 : C_1: 26.38 ; C_{15}: 71.28 ; C_5: 116.91 ; C_8 : 119.06 ; $C_{10,}$: 126.13 ; C_{11}:127.90 ; $C_{17,21}$:128.48 ;C_{19}: 129.59; $C_{18, 20}$: 130.48 ; C_{13}: 131.08; C_{12}:131.52 ; C_4: 133.49.

3- Synthesis of chalcones (3 a-j)[23]:-

The prepared 3-(2-chlorophenylazo)-4-benzyloxyacetophenone (0.91 gm, 0.0025 mol) was dissolved in 20ml of 96% ethanol, and added to the solution of an appropriate substituted benzaldehydes (0.0025 mol) in 96% ethanol (20 ml) and (2.5 ml) of 4% ethanolic sodium hydroxide. The mixture was stirred at room temperature for (1-5 min.) until the formation of pale yellow crystals of chalcone, and then kept the solution overnight at room temperature. The solid crystals were separated by suction filteration, washed with ethanol and water to neutralize, dried and purified by recrystallization from (1 : 2) xylene : ethanolthe results were illustrated in table (1)

Table 1. Melting points and yields for the prepared chalcones (3a-j).

Prod.	R	Molecular formula	M.P. / ^{0}C	% Yield
3 a	H	$C_{28}H_{21}ClN_2O_2$	103-105	85
3 b	2-F	$C_{28}H_{20}ClFN_2O_2$	122-124	86
3 c	2-Cl	$C_{28}H_{20}Cl_2N_2O_2$	128-130	93
3 d	4-Cl	$C_{28}H_{20}Cl_2N_2O_2$	138-140	75
3 e	4-F	$C_{28}H_{20}ClFN_2O_2$	161-163	97
3 f	4-Br	$C_{28}H_{20}ClBrN_2O_2$	151-152	86
3 g	4-CH_3	$C_{29}H_{23}ClN_2O_2$	157-158	60
3 h	4-OCH_3	$C_{29}H_{23}ClN_2O_3$	104-106	75
3 i	3-O-CH_2-C_6H_5	$C_{35}H_{27}ClN_2O_3$	130-131	76
3 j	3-(4-Cl-C_6H_4-CH_2O)	$C_{35}H_{26}Cl_2N_2O_3$	140-142	84

3e: ^{1}H-NMR ;5.48 (s 2H -O-CH_2-C_{22}), 7.12 (d 2H Ar-H-$C_{3,5}$), 7.15 (d 1H Ar-H-C_{12}), 7.19-7.56 (m 7H Ar-H-$C_{2,6,24,25,26,27,28}$ and 1H CH-Cα), 7.69 (d 2H Ar-H-$C_{17,20}$), 7.91 (d 1H Ar-H-C_{11}), 7.97 (d 2H Ar-H-$C_{18,19}$). 8.18 (d 1H CH-β-C_7), 8.4 (s 1H Ar-H-C_{15}). ^{13}C-NMR, 71.38**:**O-CH_2C_{22}, 114.81**:**C_{12}, 116.27**:**$C_{3,5}$, 118.03**:**$CH_\alpha C_8$, 118.44**:**C_{17}, 121.28**:**C_{15}, 127.07**:** C_{18} , 128.18**:** $C_{24,28}$, 128.71**:** C_{26} , 130.30**:** $C_{2,6}$, 130.42**:** $C_{25,27}$, 130.73**:** C_{20} , 131.21**:** C_{21} , 131.90**:** C_{19}, 133.03 **:** C_{11}, 135.49**:**C_{10}, 136.20**:** C_1, 142.27**:** C_{14} 143.28**:** CH_β C_7, 149.07**:**C_{23} 159.69 **:**C_{16}, 162.39**:** C_4 , 165.72 **:** C_{13}, 188.36**:** C=O C_9; ^{13}C- DEPT - 71.38**:**O-CH_2C_{22}, 114.81**:**C_{12}, 116.27**:**$C_{3,5}$, 118.03**:**$CH_\alpha C_8$, 118.44**:**C_{17}, 121.28**:**C_{15}, 127.07**:** C_{18} , 128.18**:** $C_{24,28}$, 128.71**:** C_{26} , 130.30**:** $C_{2,6}$, 130.42**:** $C_{25,27}$, 130.73**:** C_{20} , 131.90**:** C_{19}, 133.03 **:** C_{11}, 143.28**:** CH_β C_7.

Table 2. Reaction times, melting points and yields for the prepared pyrazolines (4a-j).

Prod.	R	Molecular formula	Time/hrs.	M.P./^{0}C	%Yield
4 a	H	$C_{28}H_{23}ClN_4O$	1.25	95-97	78
4 b	2-F	$C_{28}H_{22}ClFN_4O$	0.75	113-114	83
4 c	2-Cl	$C_{28}H_{22}ClFN_4O$	0.5	143-144	98
4 d	4-Cl	$C_{28}H_{22}Cl_2N_4O$	0.75	116-118	84
4 e	4-F	$C_{28}H_{22}ClFN_4O$	0.75	137-139	77
4 f	4-Br	$C_{28}H_{22}ClBrN_4O$	1	90-92	71
4 g	4-CH_3	$C_{29}H_{25}ClN_4O$	0.5	107-109	61
4 h	4-OCH_3	$C_{29}H_{25}ClN_4O_2$	1	66-68	79
4 i	3-O-CH_2-C_6H_5	$C_{35}H_{29}ClN_4O_2$	1	115-116	81
4 j	3-(4-Cl-C_6H_4-CH_2O)	$C_{35}H_{28}Cl_2N_4O_2$	1	95-97	86

3g: ^{1}H-NMR; 2.41 (s 3H -CH_3-C_{29}), 5.45 (s 2H -O-CH_2-C_{22}) 7.12-7.9 (m 15H Ar-H-$C_{2,3,5,6,11,12,17,18,19,20,24,25,26,27,28}$ and 1H CH-Cα), 8.19 (d 1H CH-β-C_7), 8.41 (s 1H Ar-H-C_{15}); 21.57**:**-CH_3 , ^{13}C-NMR 71.33 **:**O-CH_2C_{22}, 114.73**:** C_{12}, 118.04**:** $CH_\alpha C_8$, 118.43 **:**C_{17}, 120.54 **:**C_{15} 126.04**:** $C_{2,6}$, 127.07 **:**C_{18} , 127.36 **:**$C_{24,28}$, 128.16**:** C_{26} , 128,87**:** C_{21} , 128.92**:** $C_{25,27}$, 129.73**:** $C_{3,5}$, 130.73**:** C_{20} , 131.45**:** C_{10} , 131.87**:** C_{19} , 132.20**:** C_1, 133.06**:** C_{11} , ,

136.2: C_4 , 141.08: C_{14} , 142.25: C_{23} , 144.75: CH_β C_7 , 149.08: C_{16}, 159.58: C_{13} , 188.54 :C=O C_9; ^{13}C- DEPT

3j: ^{1}H-NMR; 5.09 (s 2H -O-CH_2-C_{22}), 5.45 (s 2H -O-CH_2-C_{29}), 7.04 (d 1H Ar-H-C_{12}), 7.23-7.83 (m 18H Ar-H-$C_{2,3,4,6,11,17,18,19,20,24,25,26,27,28,31,32,34,35}$ and 1H CH-Cα), 8.18 (d 1H CH-β-C_7), 8.45 (s 1H Ar-H-C_{15}); 69.32 :O-CH_2C_{22}, ^{13}C-NMR , 71.38 :O-CH_2C_{29}, , 114.07 :C_6 , 114.82 :C_4, 117.29 :C_{12}, 118.02 : C_2 118.51 : $CH_\alpha C_8$,121.75: C_{17}, 121.94: C_{15} , 127.08 : C_{18} ,127.39: $C_{24,26,28}$, 128.18:$C_{25,27}$ 128.72: $C_{31,35}$, 128.82: $C_{32,34}$, 130.06 :C_{20} , 130.73: C_3, 131.22: C_{10} , 131.92: C_{19}, 1133.06 :C_{11},133.89: C_{21} , 135.21: C_{33}, 135.51: C_1, 136.17: C_{14},136.43: C_{23}, 142.26: C_{30} ,144.29: CH_β C_7, 149.02 :C_{16},158.91 :C_5, 159.71: C_{13}, 188.43: C=O C_9; ^{13}C- DEPT

4- Synthesis of pyrazolines 3-[4-(benzyloxy)-3-(2-chlorophenylazo)-phenyl]-5-(substituted-phenyl)-1-substituted-2-pyrazolines(4a-j) and (5a-j)[24] :

A mixture of chalcone derivative (0.5mmoles), hydrazine hydrate (2.5mmoles) or phenylhydrazine (1mmoles) and sodium hydroxide (5ml, 0.4%) in ethanol (15ml) was refluxed with stirring for appropriate time until complete the reaction, which was monitored by either change of the color or the formation of ppt. The ppt. was isolated by suction filteration, washed with ethanol and water to neutralize, dried and purified by recrystallization from (1:2) xylene: ethanol. The physical properties and yields are summarized in table-2 .

4e: ^{1}H-NMR ;3.06 (dd 1H CH_2-H_a-C_8)**,** 3.52 (dd 1H CH_2-H_b-C_8), 4.93 (dd 1H CH-H_x-C_7), 5.43(S 2H -O-CH_2-C_{22}), 5.95 br.s 1H N-H), 7.01-7.93 (m 16H Ar-H)**;** ^{13}C-NMR ;41.5:CH_2 C_8 , 63.79: CH C_7, 71.66: O-CH_2 C_{22}, 115.38: C_{12},115.5: $C_{3,5}$, 115.79:C_{17}, 118.05: C_{15}, 126.27: C_{10}, 127.10: C_{18} , 127.30: $C_{24,28}$, 127.99: C_{26} , 128.10: $C_{2,6}$, 128.61:$C_{25,27}$, 130.24:C_{20}, 130.61:C_{19} ,131.56:C_{11}, 138.69:C_{21} , 138.42 :C_1 ,142.61:C_{14}, 149.18:C_{23}, 150.56: C_{16} , 157.05:C_9 , 160.69:C_{13} **,** 163.95 : C_4; ^{13}C- DEPT; -41.5:CH_2 C_8 , 63.79: CH C_7, 71.66: O-CH_2 C_{22}, 115.38: C_{12},115.5 :$C_{3,5}$, 115.79:C_{17}, 118.05: C_{15}, 127.10: C_{18} , 127.30: $C_{24,28}$, 127.99: C_{26} , 128.10: $C_{2,6}$, 128.61:$C_{25,27}$, 130.24:C_{20}, 130.61:C_{19} ,131.56:C_{11}.

4g: ^{1}H-NMR ;2.30 (s 3H CH_3-C_{29}), 3.09 (dd 1H CH_2-H_a-C_8), 3.58 (dd 1H CH_2-H_b-C_8), 5.25 (dd 1H CH-H_x-C_7), 5.39 (s 2H -O-CH_2-C_{22}), 5.92 (br.s 1H N-H), 6.89-7.95 (m 16 H Ar-H); ^{13}C-NMR ;21.52:CH_3 C_{29} ,41.45:CH C_8, 63.3: CH C_7, 71.43: O-CH_2 C_{22}, 114.89: C_{12}, 118.58: C_{17}, 119.54: C_{15} ,125.76: C_{10}, 126.16: C_{18}, 126.93: $C_{2,6}$, 127.11:$C_{24,28}$, 127.23: C_{26},128.56: $C_{25,27}$, 129.09: $C_{3,5}$,129.95: C_{20}, 130.45:C_{19}, 131.65:C_{11},132.92: C_{21} ,136.87: C_4, 138.18: C_{14}, 140.23:C_1, 144.24:C_{23}, 149.69:C_{16} , 152.02:C_9 , 161.38:C_{13} . ^{13}C- DEPT; -21.52:CH_3 C_{29} ,41.45:CH C_8, 63.3: CH C_7, 71.43: O-CH_2 C_{22}, 114.89: C_{12}, 118.58: C_{17}, 119.54: C_{15}, 126.16: C_{18}, 126.93: $C_{2,6}$, 127.11:$C_{24,28}$, 127.23: C_{26} ,128.56: $C_{25,27}$, 129.09: $C_{3,5}$,129.95: C_{20} ,130.45:C_{19}, 131.65:C_{11}.

4j: ^{1}H-NMR; 3.05 (dd 1H CH_2-H_a-C_8), 3.55 dd 1H CH_2-H_b-C_8), 4.95 dd 1H CH-H_x-C_7), 5.03 **(**d 2H, 1H -O-CH_2-C_{29}), 5.40 **(**d 2H, 1H -O-CH_2-C_{22}), 6.00 (br.s 1H N-H), 6.88-8.04 (m 20H Ar-H41.5:CH_2 C_8 , ^{13}C-NMR; 64.27: CH C_7, 69.19:O-CH_2 C_{22}, 71.65:O-CH_2 C_{29}, 112.64: C_4 ,114.15: C_6 , 115.38:C_{12}, 115.67: C_2, 118.06: C_{17},119.19:C_{15}, 126.35:C_{10}, 127.12: C_{18}, 127.31: $C_{24,28}$, 128: C_{26}, 128.62:$C_{25,27}$, 128.75:$C_{31,35}$,128.79:$C_{32,34}$, 130.24:C_{20}, 129.97:C_3, 130.63 :C_{19} ,131.57:C_{11}, 133.75 :C_{21}, 135.26:C_{33}, 135.39:C_{14} 136.72:C_{30} 142.61:C_{23},144.576:C_1 ,149.19:C_{16} ,150.52:C_9, 153.03:C_{13}, 158.97:C_5; ^{13}C- DEPT; -41.5:CH_2 C_8 , -64.27: CH C_7, -69.19:O-CH_2 C_{22}, -71.65:O-CH_2 C_{29}, 112.64: C_4 ,114.15: C_6, 115.38:C_{12}, 115.67: C_2, 118.06: C_{17},119.19:C_{15}, 127.12: C_{18} , 127.31: $C_{24,28}$, 128: C_{26}, 128.62:$C_{25,27}$, 128.75:$C_{31,35}$,128.79:$C_{32,34}$, 130.24:C_{20}, 129.97:C_3, 130.63 :C_{19} ,131.57:C_{11}.

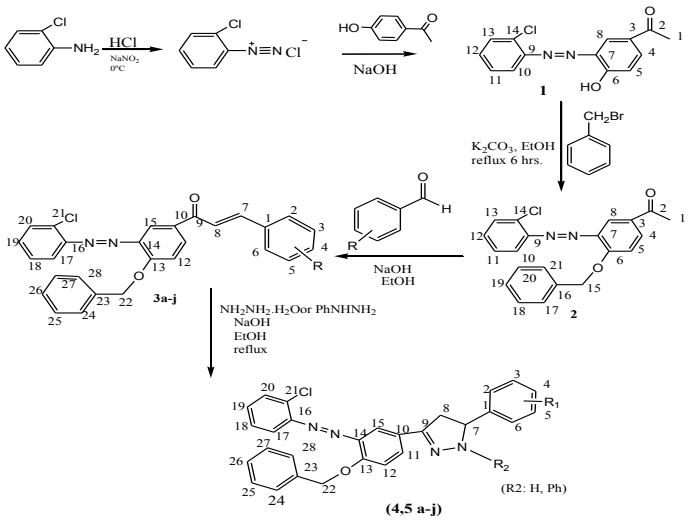
Table 3. Reaction times, melting points and yields for the prepared pyrazolines (5a-j).

Prod.	R	Molecular formula	Time/hrs.	M.P./^{0}C	%Yield
5 a	H	$C_{34}H_{28}ClN_4O$	1.5	155-156	46
5 b	2-F	$C_{34}H_{22}ClFN_4O$	2	184-186	45
5 c	2-Cl	$C_{34}H_{22}ClFN_4O$	1.25	183-184	60
5 d	4-Cl	$C_{34}H_{22}Cl_2N_4O$	2	180-182	46
5 e	4-F	$C_{34}H_{22}ClFN_4O$	1.5	189-191	48
5 f	4-Br	$C_{34}H_{22}ClBrN_4O$	1.25	140-141	50
5g	4-CH_3	$C_{35}H_{25}ClN_4O$	3	189-190	62
5 h	4-OCH_3	$C_{35}H_{25}ClN_4O_2$	1	95-96	44
5 i	3-O-CH_2-C_6H_5	$C_{41}H_{33}ClN_4O_2$	2	125-126	68
5 j	3-(4-Cl-C_6H_4-CH_2O)	$C_{41}H_{32}Cl_2N_4O_2$	2	148-149	52

5e: ^{1}H-NMR ;3.09 (dd 1H CH_2-H_a-C_8)**,** 3.82 (dd 1H CH_2-H_b-C_8), 5.22 (dd 1H CH-H_x-C_7), 5.36 (S 2H -O-CH_2-C_{22}), 7.01-7.97 (m 21H Ar-H); ^{13}C-NMR 43.04**:**CH_2 C_8 , 63.89**:** CH C_7, 71.65**:** O-CH_2 C_{22}, 113.32**:** $C_{30,34}$,114.91**:** C_{12},115.76 **:**$C_{3,5}$, 118.04**:**$C_{17,}$ 119.18**:** C_{15}, 126.13**:** C_{10}, 127.10**:** C_{18} , 127.49**:** $C_{24,28}$, 127.60**:** C_{26} , 127.98**:**$C_{25,27}$, 128.58**:** $C_{2,6}$, 128.90**:**C_{20}, 130.13**:**$C_{31,33}$,130.57**:**C_{19} ,131.59**:**C_{11}, 136.59 **:**C_{21} , 138.19 **:**C_1 ,142.58**:**C_{14}, 144.67**:**C_{23}, 146.09**:**C_{29} , 149.13**:** C_{16} , 156.88**:**C_9 , 160.46**:**C_{13} **,** 163.71 **:** C_4; ^{13}C- DEPT; -43.04**:**CH_2 C_8 , 63.89**:** CH C_7, - 71.65**:** O-CH_2 C_{22}, 113.32**:** $C_{30,34}$,114.91**:** C_{12},115.76 **:**$C_{3,5}$, 118.04**:**$C_{17,}$ 119.18**:** C_{15}, 127.10**:** C_{18} , 127.49**:** $C_{24,28}$, 127.60**:** C_{26} , 127.98**:**$C_{25,27}$, 128.58**:** $C_{2,6}$, 128.90**:**C_{20}, 130.13**:**$C_{31,33}$,130.57**:**C_{19} ,131.59**:**C_{11}.

5g: ^{1}H-NMR ;2.35 (s 3H CH_3-C_{29}), 3.15 (dd 1H CH_2-H_a-C_8), 3.85 (dd 1H CH_2-H_b-C_8), 5.25 (dd 1H CH-H_x-C_7), 5.41 (s 2H -O-CH_2-C_{22}), 6.80-7.99 (m 21H Ar-H); ^{13}C-NMR ;21**.**11**:**CH_3 C_{29} ,43.68**:**CH C_8, 64.43**:** CH C_7, 71.73**:** O-CH_2 C_{22}, 113.35**:** $C_{31,35}$, 114.94**:** C_{12}, 115.83**:** C_{33}, 118.08**:** C_{17}, 118.99**:** C_{15} ,125.84**:** C_{10}, 126.04**:** C_{18}, 127.13**:** $C_{2,6}$, 127.31**:**$C_{24,28}$, 127.99**:** C_{26} ,128.62**:** $C_{25,27}$, 128.89**:** $C_{3,5}$,129.82**:** C_{20} ,130.14**:** $C_{32,34}$,130.63**:**C_{19}, 131.54**:**C_{11},135.12**:** C_{21} ,136.56**:** C_4, 137.11**:** C_{14}, 139.45**:**C_1, 142.54**:**C_{23}, 144.76**:** C_{30}, 146.09**:**C_{16} , 149.12**:**C_9 , 156.68**:**C_{13} . ^{13}C- DEPT; 21**.**11**:**CH_3 C_{29}, -43.68**:**CH_2 C_8, 64.43**:** CH C_7, -71.73**:** O-CH_2 C_{22}, 113.35**:** $C_{31,35}$, 114.94**:** C_{12}, 115.83**:** C_{33}, 118.08**:** C_{17}, 118.99**:** C_{15} , 126.04**:** C_{18}, 127.13**:** $C_{2,6}$, 127.31**:**$C_{24,28}$, 127.99**:** C_{26}, 128.62**:** $C_{25,27}$, 128.89**:** $C_{3,5}$,129.82**:** C_{20} ,130.14**:** $C_{32,34}$,130.63**:**C_{19}, 131.54**:**C_{11}.

5j: ^{1}H-NMR ; 3.15 (dd 1H CH_2-H_a-C_8), 3.87 dd 1H CH_2-H_b-C_8), 4.96 **(**d 2H, 1H -O-CH_2-C_{29}), 5.41(dd 1H CH-H_x-C_7), 5.90 **(**d 2H, 1H -O-CH_2-C_{22}), 6.84-8.09 (m 25H Ar-H); ^{13}C-NMR ; 43.56**:**CH_2 C_8 , 64.56**:** CH C_7, 69.16**:**O-CH_2 C_{22}, 71.69**:**O-CH_2 C_{29}, 112.11**:** C_4 , 113.31**:** $C_{37,41}$, 114.05**:** C_6 , 114.94**:**C_{12}, 118.09**:** C_2, 118.67**:** C_{17},119.13**:**C_{15}, 126.25**:**C_{10}, 127.12**:** C_{18} , 127.34**:** $C_{24,28}$, 128**:**01 C_{26} , 128.63**:**$C_{25,27}$, 128.70**:**$C_{31,35}$, 128.89**:**$C_{32,34}$, 130.93**:**C_{20}, 130.15**:**C_3, 130.63 **:**C_{19} ,131.58**:**C_{11}, 133.72 **:**C_{21}, 135.21**:**C_{33}, 135.26**:**C_{14} , 136.70**:**C_{30} 142.66**:**C_{23}, 144.39**:**C_1 ,144.87**:** C_{36} ,146.07**:**C_{16} ,149.21**:**C_9, 15.92**:**$C_{13,}$ 159.20**:**C_5;^{13}C- DEPT; -43.56**:**CH_2 C_8 ,-64.56**:** CH C_7,- 69.16**:**O-CH_2 C_{22}, -71.69**:**O-CH_2 C_{29}, 112.11**:** C_4 , 113.31**:** $C_{37,41}$, 114.05**:** C_6 , 114.94**:**C_{12}, 118.09**:** C_2, 118.67**:** C_{17},119.13**:**C_{15}, 127.12**:** C_{18} , 127.34**:** $C_{24,28}$, 128**:**01 C_{26} , 128.63**:**$C_{25,27}$, 128.70**:**$C_{31,35}$,128.89**:**$C_{32,34}$, 130.93**:**C_{20}, 130.15**:**C_3, 130.63 **:**C_{19} ,131.58**:**C_{11}.



R1=H, 2-F, 2-Cl, 4-Cl, 4-F, 4-Br, 4-CH_3, 4-OCH_3, 3-$C_6H_5OCH_2$, 3-(4-Cl-$C_6H_4OCH_2$)

Scheme (1)

Results and Discussion

The synthesis of two new series of the target molecules 2-pyrazoline containing benzyloxy and azo-linkage side-chain is outlines in scheme (1). The skeleton of the synthesized compounds were confirmed by physical properties and spectroscopic methods like FT-IR, ^{1}H-NMR, ^{13}C-NMR and ^{13}C-DEPT-135. The IR spectrum of compound (1) showed a broad band at (3431) cm^{-1} attributed to (OH) group[30], a characteristic N=N band was assigned at (1557) cm^{-1} [31],two strong bands at 1679cm^{-1} and 1607cm^{-1} referring to carbonyl and carbon-carbon double bonds. The ^{1}H-NMR spectrum of compound (1) shows a singlet at (2.68) ppm for three protons of CH_3 attached to the carbonyl group, multiplet at (7.12- 8.06) and a singlet at (8.64) ppm for seven protons of the two phenyl rings and a distinct singlet signal at (12.25) ppm assigned to the hydroxyl group. ^{13}C-NMR shows twelve singlet signals corresponding to twelve types of carbon in different chemical shifts. The IR spectrum of compound (2) shows the disappearance of a broad band at (3431) cm^{-1} for hydroxyl group of 4-hydroxyacetophenone[25], and shifting the absorption band of carbonyl group from 1679 cm^{-1} to 1673 cm^{-1}, is considered as a good evidence to benzyloxation processes, two strong bands at (2927 and 2873) cm^{-1} equivalent to the (-CH_2-) group of 4-benzyloxy substrate. The^{1}H-NMR spectrum of compound (2) shows two singlet signals at (2.61 and 5.39) ppm belongs to the three protons of (-CH_3) attached to the carbonyl group and two protons of (-O-CH_2-) respectively, a multiplet signals at (7.16- 8.04) ppm, and a singlet signal at (8.45) ppm attributed to the twelve protons of aromatic rings. The ^{13}C-NMR spectrum showed three singlets at (26.38, 71.28 and 196.70) ppm belongs to the carbon atom of (-CH_3, -O-CH_2-, and carbonyl) with fourteen signals for fourteen carbons in aromatic regions. The ^{13}C-DEPT-135 of compound (2) showed upward signal at δ (26.34) for tri-protonated carbon atom of (-CH_3) group and a downward signal at (71.34) corresponding to the di-protonated carbon atom (-O-CH_2-) group with disappearance of non protonated carbon atoms . The FT-IR spectra of all chalcones (3a-j) showed the characteristic peaks of particular carbonyl functional groups[26] in the region of (1661 - 1653) cm^{-1} , the lowering

of normal (C=O) frequency from(1673) cm^{-1} indicates the presence of (C=C) conjugated to carbonyl group (conjugated enones) [27], table-4.

Table-4: Assignment of characteristic frequencies (cm^{-1}) of IR spectra for the prepared chalcones (3a-j) and pyrazolines (4 a-j), (5a-j) .

Prod.	R	Chalcones (3 a-j)		Pyrazolines (4 a-j)		Pyrazolines (5 a-j)
		C=O	C=C	C=N	N-H	C=N
A	H	1659	1605	1605	3296	1597
B	2-F	1602	1605	1603	3342	1598
C	2-Cl	1659	1604	1606	3346	1597
D	4-Cl	1661	1604	1606	3309	1598
E	4-F	1661	1595	1604	3326	1597
F	4-Br	1659	1604	1594	3335	1595
G	4-CH_3	1661	1602	1603	3334	1597
H	4-OCH_3	1653	1594	1606	3302	1597
I	3-$OCH_2C_6H_5$	1660	1600	1602	3326	1598
J	3-(4-Cl- C_6H_4-CH_2O)	1660	1595	1600	3312	1597

Table-5: Anti-bacterial activity of some prepared chalcones and pyrazolines with inhibition zone diameters in (mm) scale against *S-aureus* and *E-coli* bio-organisms.

Product no.	*E.coli* G (-ve)	*S-aureus* G(+ve)
2	6	25
3 a	8	25
4 a	11	25
5 a	25	zero
3 e	9	25
4 e	12	25
5 e	18	zero
3 f	8	25
4 f	12	25
5 f	18	zero
3 j	10	25
4 j	14	25
5 j	16	zero

The ^{1}H-NMR spectra of chalcones , show characteristic doublet signals for α, β- protons at (8.18) ppm [28], this deshielding refers to the effect of resonance of the phenyl rings that bonded to β- carbon atom, but the (CH_α) completely emerged with aromatic protons, it is

hard to distinguish it at a certain number. The ^{13}C-NMR spectra assignment of carbon atoms presented in chalcones moiety, show the characteristic peak is that related to the β-C atom nearly around (143 - 145) ppm which is more deshielded than that of α-C atom approximately at (118) ppm by the mesomeric action of carbonyl group [29]. The ^{13}C-DEPT-135 appeared a characteristic downward signal approximately at (71) ppm corresponding to the di-protonated carbon (C_{22}) atom of the (-O-CH_2-) group, and two characteristic mono-protonated carbon, at (118 and143-145) ppm belongs to (C_α and C_β) atoms respectively, and the other peaks return to Ar-C atoms. In the IR spectra of pyrazolines (4 a-j) table-4, fig.(1) exhibited a characteristic band at (3296-3346) cm^{-1} due to N-H stretching[30], also pyrazolines (5a-j) appeared strong band at (1594-1606) cm-^{1} for C=N stretching vibration , beside the appearance of above bands, the most important evidence for the formation of 2-pyrazoline is the disappearance of carbonyl group band at (1653-1661) cm^{-1}special for the chalcone moiety. The ^{1}H-NMR spectra of pyrazolines showed characteristic signals corresponding to proton of C_8 and C_7 of 2-pyrazoline ring; they form a typical ABX system confirming the nonequivalence of protons at C_8 [31]. It causes to appearance of three doublet to doublet (dd) signals approximately at (3, 3.5 and 4.7) for each compound, fig. (2) .

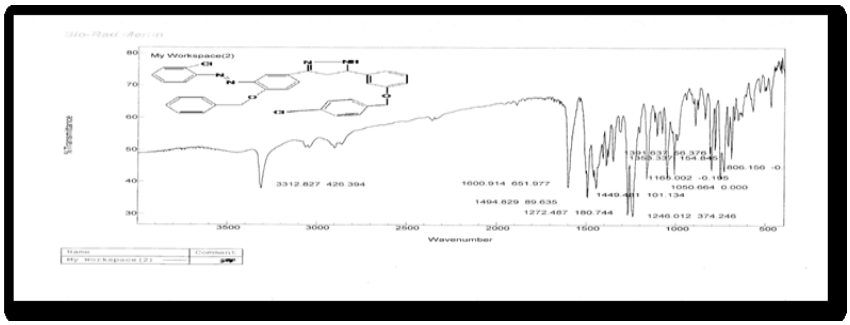


Figure 1: IR spectrum of compound (4j).

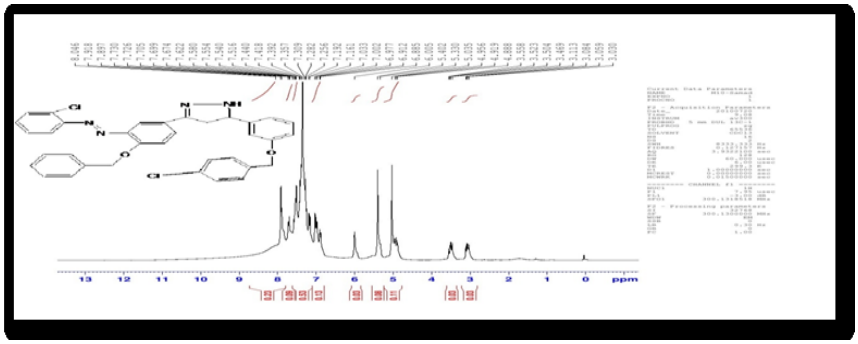


Figure 2: ^{1}H-NMR spectrum of compound (4j).

The ^{13}C-NMR spectra of pyrazolines, showed three signals approximately at, (41.5 , 63.79 and 71.66) belongs to (C_8 , C_7 and C_{22}) for pyrazoline carbon and O-CH_2 groups respectively, and the other peaks between (112 and 164) ppm approximately attributed to

aromatic carbon atoms fig(3) . The ^{13}C-DEPT-135 of pyrazolines exhibited tree downward signals at (40 , 64 and 71) ppm approximately indicated to the di-protonated carbon atoms of pyrazoline ring and two -OCH_2- group respectively, also the appearance of other upward signals corresponding to mono-protonated carbon atoms, Fig.(4)

Antibacterial Activity:

The synthesized compounds were screened for antimicrobial activity against two types of bacteria *Escherichia coli* (gram negative) and *Staphylococcus aureus* (gram positive) by using the cup-plate agar diffusion method with KBr disc of compounds .The prepared discs were placed on the surface of the cultured media with each of the two bacteria's and incubated for 24 hours at 37^{o}C and the results were monitored by measuring the zones of inhibition in mm .The screening results are listed in table (5) and they show that most of the prepared compounds are sensitive against both types of test organisms in different activities.

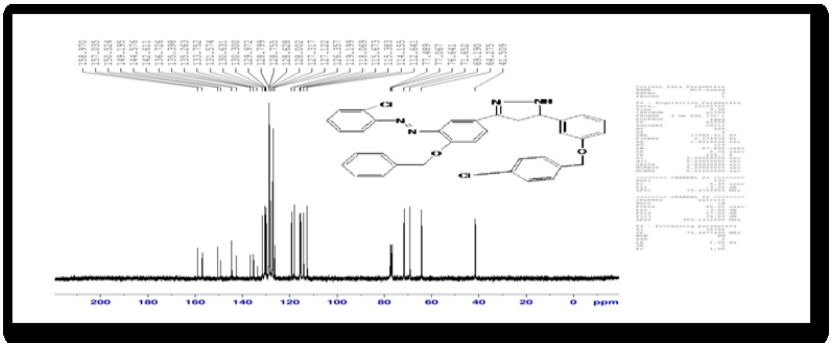


Figure 3: ^{13}C-NMR spectrum of compound (4j).

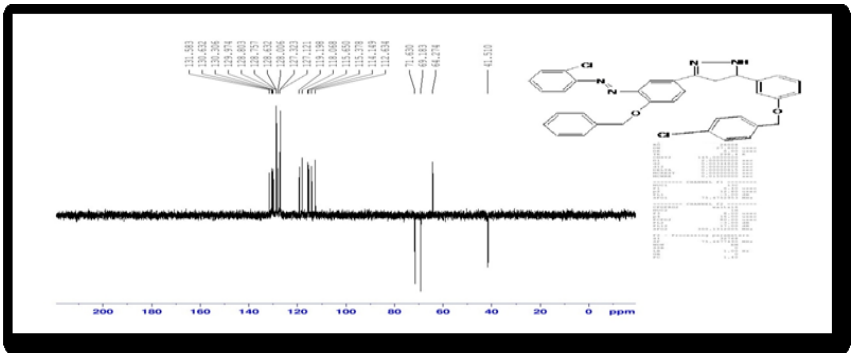


Figure 4: ^{13}C-Dept spectrum of compound (4j).

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