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ORIGINAL ARTICLE

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF NEW SCHIFF BASES

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ABSTRACT: The aim of the present study is to determine the useful of Schiff bases compounds which used as drug and antimicroble the present work involved preparation starting from3,3'-(piperazine-1,4-diyl)dipropan-1-amine a variety of schiff bases have been synthesis, all proposed structure were supported by, FT-IR, ^{1}H-NMR,^{13}C-NMR, Elemental analysis, Microbial study.

KEYWORDS: 3,3'-(piperazine-1,4-diyl)dipropan-1-amine**,** Isatin , benzophenone, acetophenone, acridin-9-one, 3-isobutyl-2,6-di(thiophen-2-yl)piperidin-4-one, Microbial Study.

INTRODUCTION

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff in 1864 (Cimerman *et al.,* 2000). The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R1, where R and R1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines (Mustapha *et al.,* 2011; Elmali *et al.,* 2000; Patel *et al.,* 1999; Valcarcel and Laque, 1994; Spichiger, 1998; Lawrence and Frei, 1976). Several studies showed that the presence of a lone pair of electrons in a sp2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents (Patai, 1970; Jungreis and Thabet, 1969; Metzler *et al.,* 1980; Adsule *et al.,* 2006) especially when a functional group like –OH or –SH is present close to the azomethine group so as to form a five or six membered ring with the metal ion. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable. Schiff bases have been known since 1864 when Hugo Schiff reported the condensation of primary amines with carbonyl compounds (Dudek, 1966). Nowadays, the research field dealing with Schiff base coordination chemistry has expanded enormously. The importance of Schiff base complexes for bioinorganic chemistry, biomedical applications, supramolecular chemistry, catalysis and material science, separation and encapsulation processes, and formation of compounds with unusual properties and structures has been well recognized and reviewed (Cimeman and Stefanac, 1985; Galic *et al.,* 1997) Isatin Schiff bases were reported to possess antiviral, anti-HIV, antiprotozoal and anthelmintic activities (Panda, 2010). They also exhibit significant anticonvulsant activity, apart from other pharmacological properties (Sondhi *et al.,* 2006).

MATERIAL AND METHODS

Schiff bases' melting points were taken on a Stuart Melting point apparatus SMP-3 and are uncorrected. Elemental analysis was carried out at Fisons EA 1108 CHNSO Micro analyzer, ^{1}H and ^{13}C -NMR spectra were determined in DMSO (internal standard TMS) on Bruker spectrometer. acetophenone, benzophenone, Isatin, acridinone were purchased from Sigma-aldrich and used without further purification. All organic solvents were purchased from Merck. By adopting the literature precedent, 3-isobutyl-2,6-di (thiophen-2-yl) piperidin-4-one were prepared (Hamak, 2013).

2.1. Synthesis of Schiff Bases

(2g,0.01 mole) of 2-amino-benzthiazole was mixed with (1.20,0.01 mole) acetophenone,

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(1.82,0.01mol) benzophenone, (1.47 gr, 0.01 mole) Isatin, (1.97 gr,0.01 mole) acridone, (3.19 gr,0.01 mole) 3-isobutyl-2,6-di(thiophen-2-yl) piperidin-4-one in 25 ml of ethanol. The resulting mixture was left under reflux for 2 hour and the solid product formed was separated by filtration, purified by recrystallization from ethanol, washed with ethanol, and then dried.

2.2. Antibacterial Testing

All the newly synthesized compounds were initially screened for their in vitro antibacterial activities against the Gram-positive (*B. subtilis, S. aureus*) and the Gram-negative (*E. coli, Salmonella spp*) were obtained from Department of Microbiology University of Damascus, Syria. The bacterial cultures were incubated at 30 ±0.1°C for 24 hours by inoculation into nutrient agar. Schiff bases were stored dry at room temperature and dissolved 20mg/ml in dimethylsulfoxide (DMSO). Antibacterial activities of each compound were evaluated by the agar well-diffusion method or bore method. Mueller Hinton Agar Media (200 cm^3) kept at 45°C was poured in the Petri dishes and allowed to solidify. Poured Petri plates (9 cm) were incubated with 50µL of normal saline solution of above culture media (105-106 bacteria per ml). Then tow well was cut out in the agar layer of each plate with an aluminum bore of 5 mm diameter. Bore injected with prepared Schiff bases (0.5 ml) were applied on the solid agar medium. The Petri plates were placed at 37°C for 24 hours. At the end of period the inhibition zones formed on media were measured with a zone reader in millimeters.

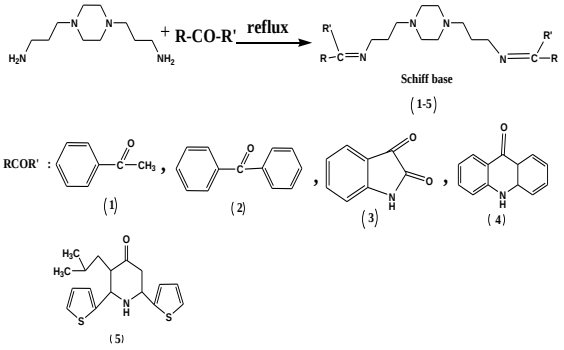
RESULTS AND DISCUSSION

3.1. Chemistry and Characterization

New five new Schiff bases have been synthesized from the condensation of 3,3'-(piperazine-1,4-diyl)dipropan-1-amine with benzophenone, acetophenone, Isatin, acridone, 3-isobutyl-2,6-di(thiophen-2-yl)piperidin-4-one (Scheme **1**). The Physical properties and the % Yield percentage of the prepared Schiff bases and elemental analysis are listed in Table (1). FT-IR, ^{1}HNMR and ^{13}C NMR spectroscopy data are listed in Tables (2,3) . FT-IR spectra of Schiff bases (1-5) showed clear absorption bands at (1648.42) Cm^{-1}due to (C=N),^{1}H-NMR spectrum Of compounds **(1-5)** show signal at (1.75,2.36,2.46 ,3.55) ppm due to protons of piperazine, ^{1}H-NMR spectrum of compound (**1**) show singlet signal at (0.9 ppm) due to (CH_3) and signals at (7.62,7.53) due to aromatic carbons. ^{1}H-NMR spectrum of compound (**2**) show signals at (7.35 ,7.58, 7.76) due to aromatic proton. ^{1}H-NMR spectrum of compound (**3**) show singlet signal at (11.18ppm) due to (NH) of Isatin in addition to signals at (7.03 7.27, 7.60 ppm) due to aromatic proton. ^{1}H-NMR spectrum of compound (**4**) show signals at (6.59, 6.75,7.14,7.51 ,7.54) ppm due to aromatic protons. ^{1}H-NMR spectrum of compound (5) show signals at (6.59, 6.75,7.14,7.51 ,7.54) ppm due to aromatic protons. ^{1}H-NMR spectrum of compound (6) shows signals at (1.75, 2.36, 2.46, 3.55, 0.66, 0.74, 1.42, 1.80) and signals at (6.93, 6.99, 7.23, 7.28) ppm due to aromatic protons. ^{13}C-NMR spectrum For compounds (1-5) show signal at (162 ppm) due to (C=N), ^{13}C-NMR spectrum For compounds (1) show signals at(0.9 ppm) due to (CH_3) and signals at (7.62,7.53 ppm) due to aromatic carbons, ^{13}C-NMR spectrum For compounds (2) show signals at(7.35 ,7.58, 7.76 ppm) due to aromatic carbons. ^{13}C-NMR spectrum of compound (3) show signal at (167.5 ppm) due to (C=O) and signals at (121.7,123.8,124.5,129.4,131.3,148.8 ppm) due to aromatic carbons. ^{13}C-NMR spectrum of compound (4) show signals at (119.2,118.4,124.7 ,130,132,142) ppm) due to aromatic carbons. ^{13}C-NMR spectrum of compound (5) show signals at (6.93, 6.99, 7.23, 7.28 ppm) due to aromatic carbons (Silverstein and Bassler, 1981).

3.2. Antibacterial Activity

The prepared Schiff's bases showed different biological activities against two types of bacteria gram positive (*B. subtilis, S. aureus*)and gram negative bacteria including (*Echerchia Coli*., *Salmonella spp)* The test results showed that the most of compounds (Schiff's) showed very good activity against gram positive and moderate activity against gram negative types of bacteria. All these results are shown in Table (4).



Scheme 1: Synthesis of new Schiff bases.

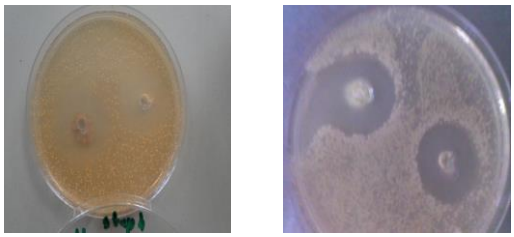


Figure 1: showing zone of inhabitation against, *S. aureus*, *Bacillus Subtillis*

CONCLUSION

Schiff bases of 3,3'-(piperazine-1,4-diyl)dipropan-1-amine with benzophenone, acetophenone, Isatin, acridone, 3-isobutyl-2,6-di(thiophen-2-yl)piperidin-4-one were synthesized and characterized by analytical and spectral techniques. These compounds exhibited good activity against *G+Ve bacteria* and moderate activity against *G-Ve bacteria*.

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Table 1: Physical properties and elemental analysis (C.H.N) for new Schiff compounds

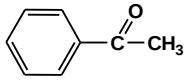
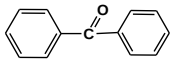
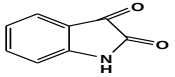
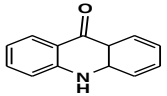
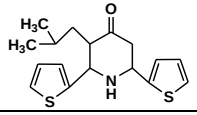
Compound	R	M.P (°C)	yield	R.F.	*Formula*	M.Wt	Calculated			Found		
							N%	H%	C%	N%	H%	C%
1		75	70%	0.87	$C_{28}H_{40}N_4$	432.64	12.95	9.32	77.73	12.09	10.19	77.72
2		96	79%	0.79	$C_{38}H_{44}N_4$	556.78	10.06	7.97	81.97	10	8.05	81.95
3		210	52%	0.69	$C_{26}H_{30}N_6O_2$	458.56	18.33	6.59	68.10	18.03	6.90	68.09
4		>300	79%	0.56	$C_{36}H_{42}N_6$	558.76	15.04	7.58	77.38	15.02	7.50	77.48
5		185	80%	0.54	$C_{44}H_{62}N_6S_4$	803.26	10.46	7.78	65.79	10.40	7.70	65.70

Table 2: FT-IR spectral data of compounds (1-5)

Comp. No.	**C=N**	**C-N**	**C-H alphatic**	**C-H arom**	***Others***
1	1648.42	1325	2890.71	3049.12	
2	1658.48	1320	2947.66	3051.8	
3	1635.26	1330.02	2950.56	3057.9	1730V(C=O) , 3240 V (N-H) amine
4	1659.74	1328.29	2957.23	3067.35	
5	1650.23	1338.25	2960.41	3060.56	

Table 3: ^{1}H-NMR and ^{13}C-NMR spectral data for prepared compounds

Compd. No.	^{1}H-NMR spectra data	^{13}C-NMR spectra data
1	0.9(s,6H,2CH_3-Ar),1.75(m,4H,2CH_2), 2.36(t,4H,2$\underline{CH_2}$-N), 2.46((m,8H,4$\underline{CH_2}$-N), 3.55((t,4H,2$\underline{CH_2}$-N=C), 7.62,7.53(m,10H,Ar)	16.4(2C,2CH_3),30.1(2C,2CH_2),52.9(4C,4CH_2-N),53.1(2C,2CH_2-N=C), 128.9,129.2,131.1 ,140.1(12C,Ar),164.6(2C,2C=N)
2	1.75(m,4H,2CH_2),2.36(t,4H,2$\underline{CH_2}$-N),2.46(m,8H,4$\underline{CH_2}$-N) ,3.55 (t,4H,2$\underline{CH_2}$-N=C) ,7.35 ,7.58, 7.76 (m,20H,Ar)	30.1(2C,2CH_2),51.7(2C,2CH_2),52.9(4C,4$\underline{CH_2}$-N),53.0(2C,2$\underline{CH_2}$-N=C), 128.9,129.2,131.1, 139 (24C,Ar), 169.2(2C,2C=N)
3	1.75(m,4H,2CH_2),2.36(t,4H,2$\underline{CH_2}$-N),2.46(m,8H,4$\underline{CH_2}$-N) ,3.55 (t,4H,2$\underline{CH_2}$-N=C),7.03 7.27, 7.60 (m,8H,Ar) 11.18(s,2H,2NH)	30.1(2C,2CH_2),51.7(2C,2CH_2),52.9(4C,4$\underline{CH_2}$-N),52.4(2C,2$\underline{CH_2}$-N=C) ,121.7,123.8,124.5,129.4,131.3,148.8 (12C,Ar),162(2C,2$\underline{C}$=N),167.5(2C,2$\underline{C}$=O)
4	1.75(m,4H,2CH_2),2.36(t,4H,2$\underline{CH_2}$-N),2.46(m,8H,4$\underline{CH_2}$-N) ,3.55 (t,4H, 2$\underline{CH_2}$-N=C),4(s,2H,2NH),6.59, 6.75,7.14,7.51 ,7.54(m,16H,Ar)	30.1(2C,2CH_2),51.7(2C,2CH_2),52.9(4C,4$\underline{CH_2}$-N),53.0(2C,2$\underline{CH_2}$-N=C),119.2,118.4,124.7 ,130,132,142.1(24C,Ar),154.3(2C,2C=N),
5	1.75(m,4H,2CH_2),2.36(t,4H,2$\underline{CH_2}$-N),2.46(m,8H,4$\underline{CH_2}$-N) ,3.55 (t,4H, 2$\underline{CH_2}$-N=C), 0.66, 0.74 (d,6H,2CH_3) , 1.42(m,2H,CH_2), 1.80 (m,1H,CH), 2.45(s,1H,NH), 2.59 (t,1H,CHC=N) , 2.68, 2.81(d,2H,CH_2), 3.99 (d,1H,CH-Ar), 4.38(t,1H,CH-Ar), 6.93, 6.99, 7.23, 7.28(6H,Ar).	30.1(2C,2CH_2),51.7(2C,2CH_2),52.9(4C,4$\underline{CH_2}$-N),53.0(2C,2$\underline{CH_2}$-N=C), 21.77(CH_3), 23.43(CH_3), 26.42(CH-(CH_3)$_2$), 33.63(CH_2-C=O), 52.22(C-3), 56.70(C-5), 57.12(C-2), 62.98(C-6), 123.83(C-2''), 124.76(C-2'), 125.63(C-3''), 126.25(C-3'), 126.67(C-1'',C-1'), 145.48(C-4''), 146.32(C-4'), 207.64(C-4).

Table 4: Microbial Study of Compound (1-5)

Comp No.	*Stap, aurea*	*Bacillus Subtillis*	*Escher. Coli*	*Salmonella spp*
1	++	++	-	-
2	++	++	±	±
3	++	++	±	±
4	++	++	±	±
5	++	++	±	-

Key the symbols :(-) = No inhibition, (±) = 6-9 mm, (++) = 15-22 mm