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SYNTHESIS AND ANTI MICROBIAL ACTIVITY OF THE DERIVATIVES OF SCHIFF BASES

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ABSTRACT

Schiff bases are compounds that have gained popularity in the paint industry because of their vibrant colours, as well as in the fields of chemistry and biochemistry because of their biological activities. Schiff bases are compounds that have gained popularity in the paint industry because of their vibrant colours, as well as in the fields of chemistry and biochemistry. Schiff bases have been extensively investigated for their potential biological applications, which include anticancer, antifungal, antibacterial, antioxidant, antituberculosis, and anthelmintic properties. Within the parameters of the investigation It has been discovered that 2-bromo-1-phenylethanone (1) and 4-chlorophenol (2) of the corresponding compound 2(4-cholrophenoxy)-1-phenylethanone (3) can be synthesized in the presence of ethanol and glacial acetic acid, respectively. It was discovered that compound (3) could be transformed to final phenoxy derivatives in the presence of amine. The newly synthesized compounds were characterized using a variety of spectroscopic techniques, including IR, 1H-NMR, and elemental analysis. The innovative approach was used to synthesise six different chemicals. The biological activity of the aforementioned chemical was investigated. All of the compounds demonstrated significant activity. Schiff bases are chemicals that have acquired appeal in the paint industry, chemistry, and biochemistry due to their biological activity. Schiff bases are chemicals that have acquired appeal in the paint business, as well as chemistry and biochemistry. Biological applications of schiff bases include anticancer, antifungal, antibacterial, antioxidant, antituberculosis, and anthelmintic characteristics. Within the scope of the study The related compounds 2(4-cholrophenoxy)-1-phenylethanone (3) and 2-bromo-1-phenylethanone (1) can be synthesized with ethanol and glacial acetic acid, respectively. In the presence of amine, compound (3) could be converted to final phenoxy derivatives. The newly synthesized compounds were characterized by infrared spectroscopy, 1H-NMR, and elemental analysis. The novel method was utilized to synthesise six compounds. The aforementioned chemical's biological activity was studied. All compounds were highly active.

INTRODUCTION

Schiff bases are well-known as important intermediates in the manufacture of a wide range of chemicals [1, 2]. When such compounds interact with nitrogen and carbon nucleophiles, a large number of physiologically active heterocyclic compounds are formed. Substituted pyrazoles, for example, have been reported to be a significant class of chemicals in the

agricultural and medicinal chemistry industries due to their wide range of biological activities [3–6] and anti-cancer properties [7]. Imidazole compounds have been found to be potent and selective neuropeptide Y Y5 receptor antagonists, as well as antifungal and antibacterial agents [8–10]. They're being looked into as potential tuberculostatic treatments. Isooxazole derivatives, on the other hand, have been shown to have antifungal activity against *Candida albicans*, as well as immunological and immunotropic properties [11–13]. Schiff bases are excellent chelating ligands with remarkable complex-forming properties. They've been used as chelating ligands for the determination of metal ions and as analytical reagents for the spectrophotometric determination of metal ions [14,15]. Several new phenoxy derivatives were obtained from 2-bromo-1-phenylethanone (1) and 4-chlorophenol (2) of corresponding compound 2(4-cholrophenoxy)-1- phenylethanone (3) were prepared in presence of ethanol and glacial acetic acid. In presence of amine compound (3) was converted to final phenoxy derivatives and their antimicrobial activity were carried out.

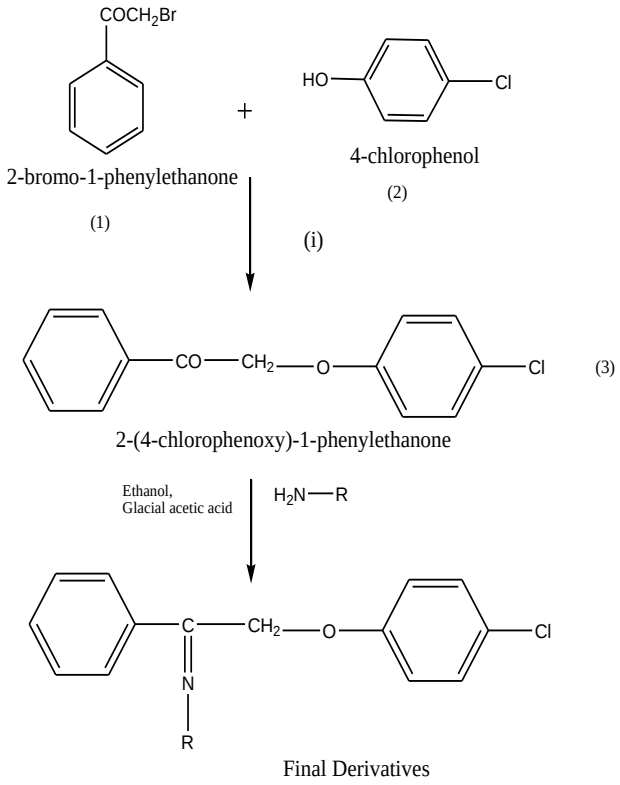
Material and methods

Procedure

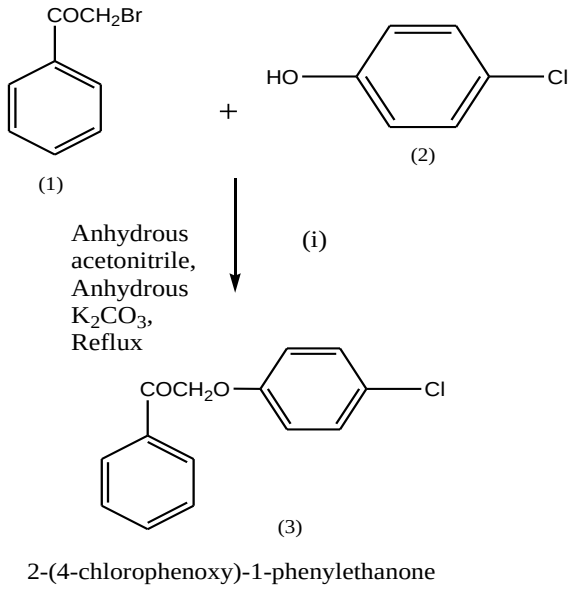
Equimolar amounts of 2-bromo-1-phenylethanone **1** (0.01mol), parachloro phenol **2** (0.01 mol) and anhydrous K_2CO_3 (0.02 mol) in dry acetonitrile was refluxed for about 10 h. The mixture was filtered and solvent was removed under reduced pressure. The resulting solid was washed with excess of water. The crude product was purified by recrystallization from ethanol to afford compound **3**.

The physical parameters were of the compounds (**3**)

Percentage yield	:	82.00%
Melting range	:	72-73 ^oC
R_f value	:	0.66
Mobile phase	:	n-Hexane: ethyl acetate: (3:1)

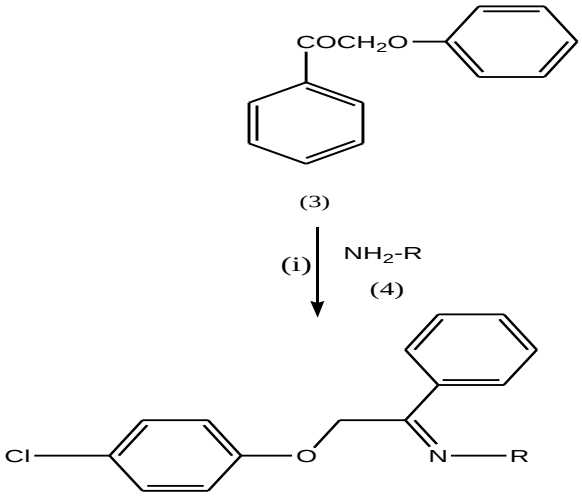


Step I. Synthesis of 2-(4-chlorophenoxy)-1-phenylethanone (3)



Reagents and conditions: (i) Anhydrous acetonitrile, Anhydrous K_2CO_3, Reflux.

Step II. Synthesis of target compounds: Schiff Bases (RS 1-4)



RS 1-4

Synthesis of the target compounds. Reagents and conditions: (i) Ethanol, Glacial Acetic Acid, Reflux.

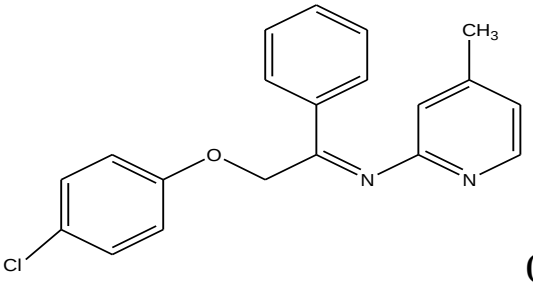
Amino compounds used the preparation of Schiff bases

Cpd. Code	Amino compounds
RS-1	2-Amino-4-methyl pyridine
RS-2	4-Amino -1, 2, 4-triazole
RS-3	2-Amino pyridine
RS-4	2-Aminothiophenol

General procedure

A mixture of compound **3** (0.01 mol), amino compound **4** (0.01mol) and 1 ml of glacial acetic acid in ethanol was refluxed on water bath for 11 h. The mixture was allowed to cool, and then the separated solid was filtered and recrystallized from ethanol to afford the **RS 1-4**.

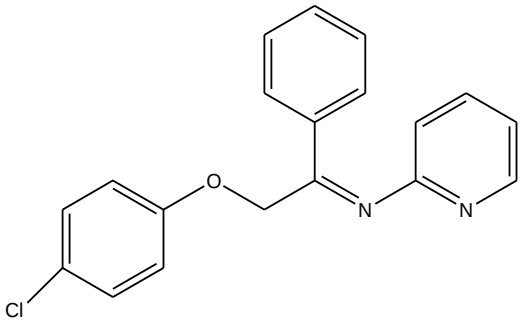
The physical parameters were of the target compounds (**RS 1-4**) were following:



(E) -N-(2-(4-chlorophenoxy)-1-phenylethylidene)-4-methylpyridin-2-amine (RS-1)

The physical parameters were of the compounds (RS-**1**)

Percentage yield : 72.00%
Melting range : 82-83 ^{o}C
R_f value : 0.80
Mobile phase : n-Hexane: ethyl acetate: (3:1)

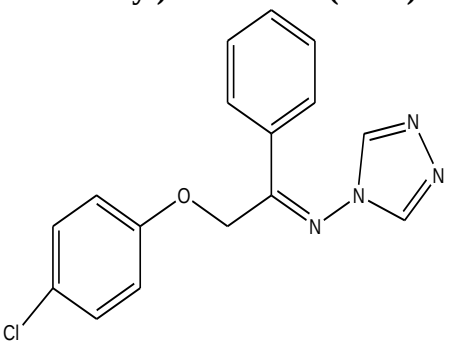


(E) -N-(2-(4-chlorophenoxy)-1-phenylethylidene) pyridin-2-amine (RS-2)

The physical parameters were of the compounds (**RS-2**)

Percentage yield : 65.00%
Melting range : 61-62 ^{o}C
R_f value : 0.76
Mobile phase : n-Hexane: ethyl acetate: (3:1)

(E)-2-(4-chlorophenoxy)-1-phenyl-N-(4H-1,2,4-triazol-4-yl)ethanimine (RS-3)

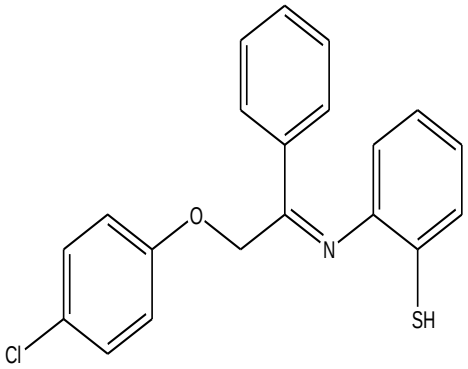


(*E*)-2-(4-chlorophenoxy)-1-phenyl-*N*-(4*H*-1,2,4-triazol-4-yl)ethanimine

The physical parameters were of the compounds (**RS-1**)

Percentage yield : 67.00%
Melting range : 74-75 ^{o}C
R_f value : 0.85
Mobile phase : n-Hexane: ethyl acetate: (3:1)

(E)-2-(2-(4-chlorophenoxy)-1-phenylethylideneamino)benzenethiol (RS-4)

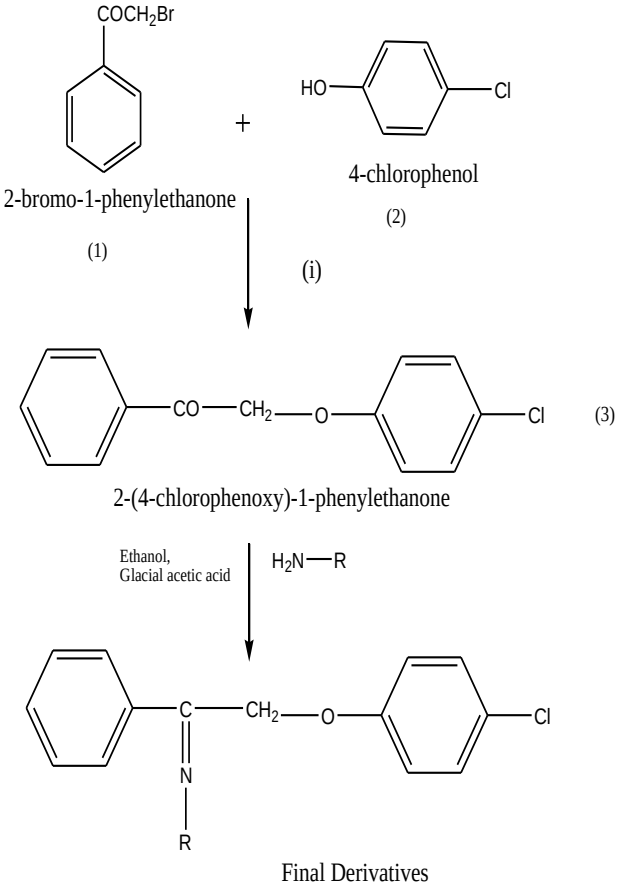


(*E*)-2-(2-(4-chlorophenoxy)-1-phenylethylideneamino)benzenethiol

The physical parameters were of the compounds (**RS-4**)

Percentage yield	:	74.00%
Melting range	:	Semi solid
R_f value	:	0.70
Mobile phase	:	n-Hexane: ethyl acetate: (3:1)

SYNTHESIS AND PHARMACOLOGICAL ACTIVITY OF NOVEL SCHIFF BASES



Antibacterial activities of all derivatives of Schiff bases were tested by the disc-diffusion method.

Preparation of test sample

Test sample of all the derivatives of Schiff bases were prepared by serial dilution method in the appropriate solvent. The residues were stored at 4°C for further use.

Test Organisms

The pure cultures of bacteria maintained in the J.S. University, Shikohabad were used for the microbiological work. The test organisms were maintained on Nutrient agar medium and Saborauld's dextrose agar medium. The test organisms were used are tabulated below: The antibacterial activity of the derivatives of Schiff bases were tested in vitro using *Staphlococcus aureus, Escherchia coli, Pseudomonas aeruginosa* and *Basillus* collected from department of microbiology, J.S. University, Shikohabad U.P. The growth Medias used were nutrient agar and nutrient broth.

Preparation of inoculums

Stock cultures were maintained at 4°C on slopes of nutrient agar. Active cultures for experiments were prepared by transferring a loopful of microorganism from the stock cultures to test tubes of nutrient broth, and incubated for 24 hrs at 37°C. The cultures were diluted with fresh nutrient broth.

Preparation of Media

The medium was prepared by dissolving the different ingredients in water and autoclaved at 121^0C for 15 minutes. This was used for preliminary antibacterial studies.

Antibacterial activity

In vitro antibacterial activity was screened by disc diffusion method using nutrient agar (NA) made from Himedia (Mumbai). The different derivatives of Schiff bases were loaded on different 3mm sterile disc till saturation. The discs were allowed to diffuse solvents for 5 minutes. The loaded disc was placed on the surface of medium containing microorganisms and the plates were kept for incubation at 37°C for 24 hrs in an incubator. At the end of

incubation, zone of inhibition formed around the disc were measured with transparent ruler in millimetre. These studies were performed in triplicate by using standard drugs (10 mcg/disc Penicillin).

Minimum Inhibitory Concentration by Serial Dilution technique

Testing was done in seeded broth containing 106 to 107 colonies forming units per ml (Cfu/ml). The crude derivatives of Schiff bases were taken at different concentrations ranging from 1000, 500, 250, 125, 62.5, 31.25 µg/ml to determine MIC by using seeded broth as diluents. Similarly, standard penicillin preparations were formulated at same concentrations as used in plant derivatives of Schiff bases. DMSO was used as solvent system for the derivatives of Schiff bases and standard drug in the experiment. The study involved a series of six assay tubes for the test compounds against each strain. In the first assay tube, 1.8 ml of seeds broth was transferred and 0.2 ml of test solution was added and mixed thoroughly to obtain a concentration of 1000 µg/ml for the derivatives of Schiff bases . To the remaining five assay tubes, 1 ml of seeded broth was transferred and then from the first assay tube, 1 ml content was pipetted out into the second assay tube and this was mixed thoroughly. This type of dilution was repeated up to 6th assay tube serially. The same procedure was followed for standard drugs. All these experimental procedures were carried out under absolute aseptic conditions. The experiments were done in triplicate. The assay tubes were then incubated at 37 ± 1^{o}C and resultant turbidities were measured using turbidity meter and MIC was calculated. Solvent controls were also observed for inhibitory action. DMSO did not show any inhibition.

For synthesized compound, an MIC below 100 µg/mL was considered as an excellent effect, 100 to 500 µg/mL as moderate, 500 to 1000 µg/mL as weak and over 1000 µg/mL as inactive.

Antimicrobial susceptibility test

The disc diffusion method was used to screen the antimicrobial activity. In vitro antimicrobial activity was screened by using Nutrient agar (NA) obtained from Himedia (Mumbai). The NA plates were prepared by pouring 15 ml of molten media into sterile petriplates. The plates were allowed to solidify and 0.1 % inoculum suspension was swabbed uniformly and the inoculum was allowed to dry for 5 minutes. The different derivatives of Schiff bases were loaded on 3mm sterile disc till saturation. The loaded disc was placed on the surface of medium and the compound was allowed to diffuse for 5 minutes and the plates were kept for incubation at 37°C for 24 hrs. At the end of incubation, inhibition zones formed around the disc were measured with transparent ruler in millimeter. The same procedure was followed by using Saborauld's dextrose agar plates for the fungus also. These studies were performed in triplicate by using standard drugs (10 µg/disc Penicillin; for bacteria)

Result and discussion

Antimicrobial activity of derivatives of Schiff bases.

The derivatives of Schiff bases were subjected to antibacterial activity using different micro organisms (*Bacillus subtilis*, *Staphylococcus aureus*; *Pseudomonas aeruginosa* and *Escherichia coli*). The result was tabulated in the table 1 & 2. It showed that all the four compound have moderate activity against all test organism with the standard drugs Penicillin was co-assayed for comparison.

Table 1. Zone of inhibition of different derivatives of Schiff bases

S.N.	Zone of inhibition of different derivatives of Schiff bases in mm							
	Compound	**Test organisms**	**1000 µg/ml**	**500 µg/ml**	**250 µg/ml**	**125 µg/ml**	**62.5 µg/ml**	**STD Penicillin**
1	RS-1	*TO1(E coli)*	7	5	6	4	1	10
2		*TO 2(P. aureginosa)*	6	4	2	0	0	
3		*TO 3 (S. aeurus)*	5	5	0	3	2	
4		*TO 4(Bacillus).*	7	6	6	5	3	
5	RS-2	*TO1(E coli)*	5	3	1	1	0	
6		*TO 2(P. aureginosa)*	3	2	0	0	0	
7		*TO 3 (S. aeurus)*	7	6	6	6	3	
8		*TO 4(Bacillus).*	6	6	6	3	1	
9	RS-3	*TO1(E coli)*	7	4	3	1	0	
10		*TO 2(P. aureginosa)*	8	6	5	3	2	
11		*TO 3 (S. aeurus)*	7	5	4	2	2	
12		*TO 4(Bacillus).*	7	7	5	4	3	
13	RS-4	*TO1(E coli)*	8	5	4	5	1	
14		*TO 2(P. aureginosa)*	8	6	6	5	4	
15		*TO 3 (S. aeurus)*	7	7	5	3	3	
16		*TO 4(Bacillus).*	8	8	7	4	3	

Table 2. Minimum Inhibitory Concentration of different derivatives of Schiff bases in various solvent µg/ml.

S.N.	Minimum Inhibitory Concentration of different derivatives of Schiff bases in µg/ml							
	Compound	**Test organisms**	**N hexane**	**Ethyl acetate**	**acetone**	**Ethanol.**	**methanol**	**STD Penicillin**
1	Rs-1	*TO1(E coli)*	1000	1000	500	1000	500	31.25
2		*TO 2(P. aureginosa)*	500	1000	500	500	62.5	
3		*TO 3 (S. aeurus)*	1000	1000	ND	1000	1000	
4		*TO 4(Bacillus).*	1000	ND	500	500	250	
5	Rs-2	*TO1(E coli)*	ND	1000	1000	500	500	

6		*TO 2(P. aureginosa)*	1000	500	ND	ND	500	
7		*TO 3 (S. aeurus)*	500	500	500	500	1000	
8		*TO 4(Bacillus).*	500	ND	500	1000	500	
9	Rs-3	*TO1(E coli)*	ND	1000	1000	500	500	
10		*TO 2(P. aureginosa)*	500	500	ND	500	500	
11		*TO 3 (S. aeurus)*	500	500	1000	500	500	
12		*TO 4(Bacillus).*	1000	500	ND	1000	500	
13	Rs-4	*TO1(E coli)*	500	1000	1000	500	500	
14		*TO 2(P. aureginosa)*	500	500	500	1000	500	
15		*TO 3 (S. aeurus)*	500	500	500	ND	500	
16		*TO 4(Bacillus).*	1000	ND	500	1000	ND	

Most of the compound showed moderate activity towards microorganism. Further antioxidant antifungal activity and antibacterial activity using different microorganism may be perform in future.

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