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Original Research Article

DESIGN AND PHARMACOLOGICAL EVALUATION OF NEW SCHIFF BASES AS POTENTIAL THERAPEUTIC AGENTS

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Abstract: A series of novel Schiff bases (NSB-1 to NSB-4) were synthesized and evaluated for their antimicrobial activity. The structures of the synthesized compounds were confirmed by melting point determination, thin-layer chromatography (TLC), infrared (IR) spectroscopy, and 1H-NMR spectral analysis. The antimicrobial activity of the title compounds was assessed against Bacillus subtilis (Gram-positive), Escherichia coli (Gram-negative), and Candida albicans. Ampicillin and clotrimazole were used as standard reference drugs for comparison. Among the tested compounds, NSB-4 exhibited the highest antimicrobial activity, showing a maximum zone of inhibition of 20 mm against B. subtilis. The results suggest that these Schiff base derivatives possess promising antimicrobial potential.

Keywords: Amino compounds, antimicrobial activity and Schiff base.

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INTRODUCTION

Schiff bases are compounds containing an imine or azomethine (–C=N–) functional group. They are typically formed by the condensation reaction of primary amines with carbonyl compounds and were first reported by Hugo Schiff. Infectious diseases continue to pose a major global health challenge, particularly in developing and underdeveloped countries. In addition, the increasing ability of microorganisms to develop resistance to existing antibiotics has intensified the need for the discovery and development of novel antimicrobial agents. The imine functional group present in Schiff bases has been shown to play a crucial role in a wide range of biological activities, with antibacterial and antifungal properties being especially prominent. In light of these observations and the growing threat of antimicrobial resistance, the present study focuses on the synthesis and antimicrobial evaluation of some new Schiff base derivatives.

EXPERIMENTAL

The melting points of the synthesized compounds were determined by the open capillary method and are uncorrected. The infrared (IR) spectra of the synthesized compounds were recorded in potassium bromide (KBr) discs using a Perkin Elmer RX1 spectrophotometer. The progress of the reactions was monitored by thin-layer chromatography (TLC) using silica gel G, and the spots were visualized under iodine vapor. All the target compounds were subjected to biological evaluation for antimicrobial activity.

Synthesis of Schiff Bases

Step I. Synthesis of 2-(4-chlorophenoxy)-1-phenylethanone(3) $C_{14}H_{11}ClO_2$

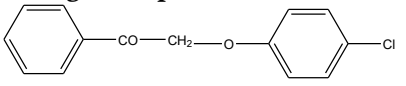
Procedure

Equimolar amounts of 2-bromo-1-phenylethanone **1** (0.01mol), 4-chloro phenol **2** (0.01 mol) and anhydrous K_2CO_3 (0.02 mol) in dry acetonitrile was refluxed for about 6 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**. **(Molecular Formula - $C_{14}H_{11}ClO_2$)**

IR Spectra value of 2-(4-chlorophenoxy)-1-phenylethanone (3)

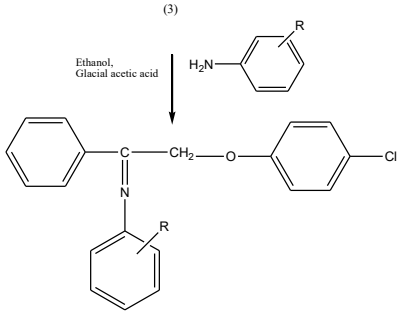
S.No.	ν (cm^{-1})	Functional Group
1.	3082	CH Str. Aromatic
2.	2917	CH Str. Aliphatic
3.	1701	C=O str.
4.	1595	C=C str. in aromatic
5.	1089	C-O str. in C-O-C

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



2-(4-chlorophenoxy)-1-phenylethanone

(3)



Synthesis of the target compounds.

Reagents and conditions: (i) Ethanol, Glacial Acetic Acid, Reflux.

Amino compounds used the preparation of Schiff bases-

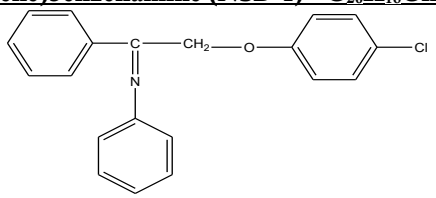
Cpd. Code	Amino compounds
NSB-1	Aniline
NSB-2	3-nitro aniline
NSB-3	4-nitro aniline
NSB-4	2-choloro-3-nitro aniline

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 10 h. The mixture was allowed to cool, and then the separated solid was filtered and recrystallized from ethanol to afford the **NSB-1 to NSB-4**.

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

N-(2-(4-chlorophenoxy)-1-phenylethylidene)benzenamine (NSB-1) - $C_{20}H_{16}ClNO$



N-(2-(4-chlorophenoxy)-1-phenylethylidene) benzenamine

S.No.	ν (cm^{-1})	Functional Group Assignment
1.	3065	CH Str. Aromatic
2.	2901	CH Str. Aliphatic
3.	1433	C=N str.
4.	1095	C-O str. in C-O-C

IR Spectra value of N-(2-(4-chlorophenoxy)-1-phenylethylidene) benzenamine (NSB-1).

N-(2-(4-chlorophenoxy)-1-phenylethylidene)-3-nitrobenzenamine (NSB-2)- $C_{20}H_{15}ClN_2O_3$

S.No.	ν (cm^{-1})	Functional Group
1.	3062	CH Str. Aromatic
2.	2901	CH Str. Aliphatic
3.	1175	C-N str.
4.	1430	C=N str.
5.	1093	C-O str. in C-O-C

IR Spectra value of (N-(2-(4-chlorophenoxy)-1-phenylethylidene)-3-nitrobenzenamine (NSB-2) N-(2-(4-chlorophenoxy)-1-phenylethylidene)-4-nitrobenzenamine (NSB-3)- $C_{20}H_{15}ClN_2O_3$

S.No.	ν (cm^{-1})	Functional Group
1.	3062	CH Str. Aromatic
2.	2906	CH Str. Aliphatic
3.	1175	C-N str.
4.	1432	C=N str.
5.	1092	C-O str. in C-O-C

IR Spectra value of N-(2-(4-chlorophenoxy)-1-phenylethylidene)-4-nitrobenzenamine (NSB-3)

N-(2-(4-chlorophenoxy)-1-phenylethylidene)-2-chloro-3-nitrobenzenamine (NSB-4) -$C_{20}H_{14}Cl_2N_2O_3$

S.No.	ν (cm^{-1})	Functional Group
1.	3069	CH Str. Aromatic
2.	2907	CH Str. Aliphatic
3.	1433	C=N str
4.	1178	C-N str.
5.	1089	C-O str. in C-O-C

IR Spectra value of N-(2-(4-chlorophenoxy)-1-phenylethylidene)-2-chloro-4-nitrobenzenamine (NSB-4)

DETERMINATION OF ANTIMICROBIAL ACTIVITY:

The antimicrobial testing was performed using the cup diffusion technique. The synthesized compounds, as 1 mg/ml solutions in dimethylformamide (DMF), were evaluated *in vitro* for activity against *C. albicans* by the cup diffusion technique. Compounds showing inhibitory zones of at least 20 mm were considered active. Ampicillin and Clotrimazole were used as standard antimicrobial agents. Dimethylformamide was used as a control. Sterile nutrient agar was inoculated with the test organisms (each 100 mL of the medium received 1 mL of 24 h broth culture), and then seeded agar was poured into sterile petri dishes. Cups (8 mm in diameter) were cut in the agar, and each cup received 0.1 mL of the test compound solution. The plates were then incubated at 37°C for 24 h. The activities were estimated as zones of inhibition in mm diameter. Ampicillin and Clotrimazole solutions (0.01%) were used as reference standards. DMF did not show any inhibition zones.

The Antimicrobial Activity of Schiff bases (NSB-1 to NSB-4)

Cpd.Code	Zone of Inhibition (in mm) against *B. Subtilis*	Zone of Inhibition (in mm) against *E. Coli*	Zone of Inhibition (in mm) against *C. Albicans*
NSB-1	17	17	17
NSB-2	15	15	19
NSB-3	16	17	19
NSB-4	20	19	17
Ampicillin	27	25	-
Clotrimazole	-	-	25

The compounds having zone of inhibition 20 or greater 20 mm is considered as active.

RESULTS AND DISCUSSION

The results of the Schiff bases containing atoms chloro at 2 position and nitro at 3 position was showing most potent antibacterial activity against B. Subtilis as compared to the other Schiff bases but none of Schiff base was active against E.Coli and C.Albicans bacteria. Among the compound NSB-4 was showed most potent antifungal activity (20mm) against B. Subtilis in the test compounds.

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