SYNTHESIS AND ANTIMICROBIAL EVALUATION OF SOME NOVEL AND BIOLOGICALLY ACTIVE SCHIFF BASES BEARING A 1,3,4-THIADIAZOLE MOIETY

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Abstract

A new series of Schiff base derivatives bearing 134 Thiadiazole moiety were synthesized by reaction of 2-amino, 5-ethyl, 134 Thiadiazole with substituted aromatic aldehydes. The structure of all the Schiff bases were characterized using FT-IR, NMR spectroscopy and elemental analysis. The antibacterial activity of these compounds were investigated against Staphylococcus aureus (RTCC, 1885), and Escherichia coli (ATCC, 35922).

Keywords: Schiff base, 1,3,4-thiadiazole, biological activities

1. INTRODUCTION

There has been considerable attention to the chemistry of Schiff bases because of their wide range of applications in many fields including biological, organic, inorganic and analytical chemistry. They are used as pigments, dyes, catalysts, intermediates in organic and inorganic synthesis and a activities.5-11 Furthermore, some Schiff bases are used in ion sensors and electrochemical sensors to empower detection with enhanced selectivity and sensitivity.12,13

Due to the importance and diverse structural aspects of Schiff bases, several methods and procedures have been reported for synthesis of these compounds.14-19 These methods usually involve the straightforward acid-catalyzed reaction of a primary amine and a carbonyl group in organic solvents. However, in spite of their advantages, most of them use procedures in which the chemical safety and yields of products are the main considerations. Hardly ever has attention been concentrated on the fact that some of these established methods use toxic solvents, special apparatus, or strong acid conditions. Consequently, in order to overcome these limitations, the introduction of more efficient methods for the synthesis of Schiff bases is still a challenge. Recently, significant research has been directed toward the solvent-free reaction in order to improve classical procedures and make them cleaner and easier to carry out.20, 21 Keeping these reports in mind and also due to our interest in the synthesis of Schiff bases16,22-24 we wished to study the synthesis of some novel and biologically active Schiff bases bearing a 1,3,4-thiadiazole moiety under both solvent-free and acidic conditions.

Therefore, we have synthesized some substituted Schiff bases of 5-ethyl-1,3,4-thiadiazole-2-amines and studied their antimicrobial activities.

2. EXPERIMENTAL

2. 1. General

Chemical used in this present study were procured from Sigma-Aldrich and E-Merck chemical companies. The melting point of all compounds were determined in open glass capillaries on V-SCIENTIFIC MP-DS melting point apparatus and are uncorrected.

The infrared spectra of all compounds were recorded in KBr discs on Thermo scientific NicoletiS5, US made Fourier transform spectrophotometer.

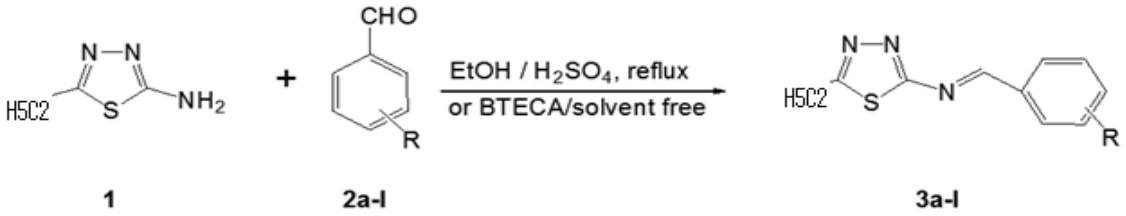
The NMR spectra of selective compounds were recorded in BRUKER AV 400

spectrometer operating at 400 MHz for $_{1}H$ NMR spectra and 100 MHz for $_{13}C$ NMR spectra in $CDCl_3$ solvent using TMS as internal

standard. Mass spectra of all synthesized products were recorded on SHIMADZU mass spectrometer using chemical ionization technique.

2. 2. General procedure for synthesis of substitutedbenzylidene-5-ethyl-1,3,4-thiadiazole-2-amines:

To a mixture of 2-amino-5-ethyl-1,3,4-thiadiazole **1** (0.133 g, 1mmol) and corresponding aromatic aldehyde **2** (1mmol) in ethanol (10 ml) was added 3-4 drops of concentrated sulfuric acid. The reaction mixture was refluxed for an appropriate time as presented in Table 1. After completion of the reaction, controlled by TLC, the reaction mixture was cooled to room temperature giving a solid product after 10-30 min, which was filtered and washed with a mixture of hot water and ethanol (1:1, 10 ml) to afford the pure product **3.**



Scheme 1. Preparation of Schiff bases 3a-l

2.3. ***Antibacterial study***

The agar diffusion test, or Kirby-Bauer disk-diffusion method was used for this purpose. Each chemically synthesized material (5 mg) was dissolved in 250 µl of DMSO and 100 µl of the solution of the test compounds was introduced onto the disks (0.7 cm diameter). The disks were then placed on top of the medium previously inoculated with the bacteria. 100 µl of solvent (DMSO) was added to another disk and implanted as a negative control on each plate along with the standard drugs. The plates were incubated overnight at 37°C. The inhibition zones were measured and compared with the controls. For the zone size interpretations were used recommendations of the National Committee of Clinical Laboratory Standards (NCCLs). The results are given in Table 2.

3. Result and Discussion

The synthesized Compounds were characterized by their physical constants, IR, ^{1}H and ^{13}C NMR and Mass spectral data.

Table 1. Synthesis of Schiff bases 3a-l under acidic conditions

Entry	R	Product	Time (Min.)	Yield (%)
1	H	3a	30	80
2	2-OH	3b	35	60
3	2-OMe	3c	45	65
4	2-Cl	3d	40	68
5	2-OH, 5-Br	3e	60	70
6	3-Br	3f	55	57
7	4-Isopropyl	3g	60	74
8	4-NMe_2	3h	75	65
9	4-NO_2	3i	80	67
10	4-OCH_2Ph	3j	90	68
11	4-Cl	3k	70	62
12	4-F	3l	45	64

All compounds form yellow crystals except for **3d** and **3h** which are white and orange, respectively. The good yields of products, the use of safe and mild reaction conditions and the shorter reaction time are some advantages of the method for the synthesis of Schiff bases in the presence of Sulfuric acid.

IR and NMR spectra data as well as elemental analyses are consistent with the expected structures. In the 1H NMR spectra of all the Schiff bases synthesized here, the appearance of singlets at 8.41-8.98 and 14.26-14.71 ppm related to the resonance of vinyl and SH protons, respectively, is good evidence for the expected reactions. Also, In the IR spectra of compounds **3a-l** the absence of the absorption related to the NH2 group of the starting material is in support of the reactions having taken place.

The antibacterial screening data revealed that none of the compounds showed antibacterial activity against *E. coli*, as an example of gram negative bacteria (Table 2).

Table 2: Inhibition zone diameter for Schiff bases 3a-l.

Entry	Compounds	*S. aureus* (mm)	*E. coli* (mm)
1	**3a**	—	—
2	**3b**	15±0.1	—
3	**3c**	25±0.2	—
4	**3d**	7±0.1	—
5	**3e**	32±0.2	—
6	**3f**	9±0.1	—
7	**3g**	8±0.2	—
8	**3h**	29±0.2	—
9	**3i**	17±0.1	—
10	**3j**	17±0.1	—
11	**3k**	—	—
12	**3l**	9±0.1	—
13	**DMSO**	—	—
Gentamicin 18mm	10 U Penicillin 33 mm	Standard drugs	Standard drugs

-indicates resistance of bacteria to compounds. The inhibition zone numbers are the averages of three independent experiments.

It was observed that Compounds **3b-j** and **3l** showed good inhibition against *S. aureus* comparable to penicillin. Also, the anti-*S. aureus* activity of compounds **3c, 3e** and **3h** is better than that of the other compounds.

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