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FACILE AND EFFICIENT METHOD FOR PREPARATION OF SCHIFF BASES CATALYZED BY Ni $(NO_3)_2.6H_2O$ UNDER ROOM TEMPERATURE

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ABSTRACT

The important and interesting roles of Schiff bases are an intermediate in the biologically important transmutation reaction. Heterocyclic Schiff bases have been reported as antibacterial and antifungal activities. They were synthesized by different methods by the condensation between primary amines and aldehyde or ketones. From literature survey, it was cleared that many work on Schiff bases is going on. But each work is only concerns with conventional method and grinding method. But very few reports were observed on synthesis of Schiff bases by green approach. Therefore, in present work some Schiff bases were prepared with help of aromatic primary amines and highly substituted aromatic aldehydes in methanol and in presence of Ni $(NO_3)_2.6H_2O$ as catalyst at room temperature.

Key words: Schiff bases, Aldehyde, Ketones, Biological activity, Catalyst.

INTRODUCTION

Schiff bases derived from aromatic amines and aromatic aldedydes are a very important class of organic compounds because of their applications in many fields, including biological[1-9], inorganic[10-14] and analytical chemistry[15-19]. The chemistry of the carbon-nitrogen double bond plays a vital role in the progresses of chemistry science[20]. Schiff-base compounds have been used as fine chemicals and medical substrates. Recently multi-dentate complexes of iron and nickel showed high activities of ethylene oligomerization and polymerization. Studies on the bioavailability of heterocyclic Schiff bases from natural sources are limited, but synthetic heterocyclic Schiff bases have been reported to have a wide range of biological properties, especially antibacterial[4,21,22] and antifungal activities[5].

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From above literature survey, it was cleared that many work on benzyldine was going on. But each work is only concerns with conventional method and grinding methods. But very few reports were absorbed on synthesis of benzylidine by green approach. Therefore in present work, some benzylidine were prepared with help of aromatic primary amines and highly substituted aromatic aldehydes in methanol and presence of $Ni(NO_3)_2.6H_2O$ as catalyst at room temperature.

The aim of this research project was to screen simple and economic methods for preparation of Schiff-bases. Here in $Ni(NO_3)_2.6H_2O$ promoted condensation reaction of highly substituted aldehyde and aryl amines displayed the convenient practicing way for forming a series of Schiff bases Scheme.

Synthesis of Schiff base is often carried out with acid-catalyzed and generally by refluxing the mixture of aldehyde and amine in organic medium. However, with the assistance of $Ni(NO_3)_2.6H_2O$, it was found that the condensation reaction of highly substituted aldehyde and various aryl amines could proceed fast and efficiently (Table 1). The products could be purified simply by re-crystallization in an appropriate ethanol. The yields of products were high.

EXPERIMENTAL

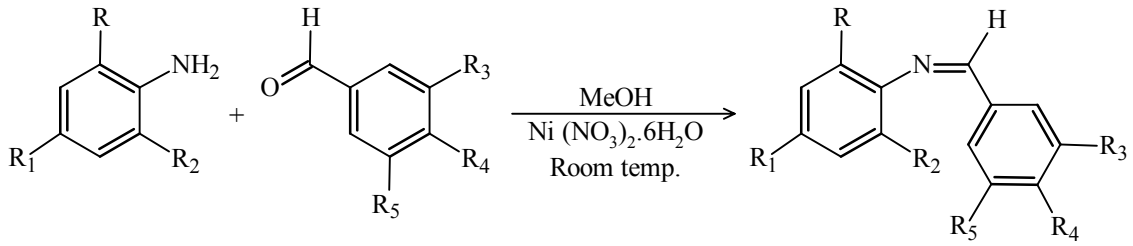
All chemicals used were purchased from S. D. fine Chemicals. Melting points were determined in open capillary tubes and are uncorrected. The purities of the compounds were checked on silica-gel-coated Al plates. IR spectra were performed on a Galaxy series FTIR 5000 spectrometer using KBr discs. NMR spectra were recorded on a Bruker (300 MHz) spectrometer. Chemical shifts (ppm) were referenced to the internal standard tetramethyl silane (TMS).

General preparation of Schiff bases (3a-f)

To a solution of aromatic aniline (0.01 mol) in methanol (5 mL), corresponding highly substituted aromatic aldehyde (0.01 mol) was added. Then $Ni(NO_3)_2.6H_2O$ (5 mol %) was added and the reaction mixture stirred at room temperature for the desired time. After completion of the reaction, cold water (15-25 mL) was added to give the product. The solid product was filtered and washed with cold water and air dried (Scheme).

Antimicrobial activity

All of the novel synthesized compounds were screened for their antimicrobial activity against the Gram –ve bacteria *Escherichia coli* (ATCC 8739) and Gram +ve bacteria *Staphylococcus aureus* (ATCC6538).



(1) **(2)** **(3)**

Scheme

The prepared compounds (1.5 g) were dissolved in chloroform (25 mL) to obtain the solutions (60 mg/mL) and further concentrations (20 and 10 mg/mL) were obtained by dilution method. The solutions were sterilized by filtration by 0.45 m Millipore filters. Antimicrobial tests were then carried out by using the disc diffusion method. One hundred micro liters of suspension containing 108 CFU/mL of bacteria were spread on Muller-Hinton agar (MHA) medium. The discs (6 mm in diameter) were impregnated with 10 L of the solutions (60, 20, 10 mg/mL). Negative controls were prepared by using the same solvent (chloroform), employed to dissolve the test compounds. A known antibiotic, Ofloxacin 10 L of solution (5 mg/mol), was used as positive reference standard. The loaded discs were then placed in the above-prepared plates. The inoculated plates were incubated at 37^{o}C for 24 hours. Antimicrobial activity was evaluated by measuring the diameter (mm) of zone inhibition Table 2.

RESULTS AND DISCUSSION

A variety of methods have been reported for the preparation of this class of compounds. Schiff bases were prepared in this work through condensation of aniline, substituted aniline and highly substituted chloro, bromo and methoxy derivatives of aromatic aldehydes by using $Ni(NO_3)_2.6H_2O$ (5 mol %). Yield of Schiff bases was 50-84%. This method also reduces reaction time. The physical data of benzylidine compounds were given in Table 1. The IR, NMR, mass and elemental analysis data confirmed their molecular structure. All Schiff bases showed different effects on bacterial species. The results, recorded as average diameter of inhibition zone in mm, are given in Table 2.

It shows the mean of inhibition zone of some Schiff bases, which were tested at different concentrations against species of human pathogenic bacteria. The results from this

study indicated that some Schiff bases had antibacterial activities against *E. coli* and *S. aureus*. In contrast, no effect was observed of **3b** and **3d** compounds against bacteria tested. It can be conclude that compound **3a** has antibacterial activity more efficient than the standards used in this research work.

Table 1: Physical data of Benzylidine compounds

Comp.	R	R_1	R_2	R_3	R_4	R_5	M.P. (^{0}C)	Yield[a]
3a	H	H	H	H	H	OMe	176	76
3b	H	NO_2	H	OMe	OMe	OMe	250	84
3c	NO_2	I	H	Br	OMe	OMe	134	78
3d	I	NO_2	H	H	OMe	OMe	252	50
3e	H	Cl	H	Br	OMe	OMe	160	68
3f	H	Cl	H	OMe	OMe	OMe	110	75
3g	I	NO_2	H	OMe	OMe	OMe	145	68

a = Isolated yield after purification

Table 2: Antimicrobial screening results of the Benzylidine derivatives (3a-g)

Entry	Compounds	Bacteria	
		***E. Coli* ATCC 8739**	***S. Aureus* ATCC 6538**
1	3a	14 mm	10 mm
2	3b	-	8 mm
3	3c	14 mm	10 mm
4	3d	8 mm	-
5	3e	10 mm	6 mm
6	3f	8 mm	10 mm
7	3g	11	8.5 mm
Ofloxacin	Ref.	15	12

Spectral analysis

Compound (3c): (Z)-N-(3-Bromo-4, 5-dimethoxybenzylidene)-4-iodo-2-nitro-benzenamine yellow solid; M.P. 134^{o}C; yield-78%; FT-IR (KBr): 3076 (w), 2959 (m), 1621 (s), 1675 (s), 1405 (m), 1113 (w), 840 (s) and 688 (m) cm^{-1} ^{1}H NMR (300 MHz, DMSO-d6) δ : 3.80 (s, 3H, OMe); 3.87 (s, 3H, OMe) 7.20-8.36 (m, 6H, Ar-H) 11.71 (s, 1H, NH), 9.28 (s, 1H,CH) .MS: 490; $C_{15}H_{12}BrIN_2O_4$; calcu, C, 36.67, H, 2.53, Br, 13.97, I, 25.78, N, 5.98, O, 12.98, found; C, 36.60, H, 2.50, Br, 13.90, I, 25.81, N 6.00, O, 12.97

Compound (3d): (Z)-N-(3,4dimethoxybenzylidene)-2-iodo-4-nitrobenzenamine yellow solid; M.P. 152^{o}C; Yield-50%; FT-IR (KBr): 3066 (w), 3019 (m), 1618 (s), 1670 (s), 1409 (m), 1083 (w), 788 (s) and 678 (m) cm^{-1} ^{1}H NMR (300 MHz, DMSO-d6) δ : 3.72 (s, 3H, OMe); 3.77 (s, 3H, OMe) 7.28-8.42 (m, 5H, Ar-H) 11.71 (s, 1H, NH), 9.28 (s, 1H, CH). MS: 490; $C_{15}H_{13}IN_2O_4$; calcu, C, 40.94, H, 3.20, I, 31.00, N 6.90, O, 15.58, found; C, 40.90, H, 3.18, I, 30.90, N 6.92, O, 15.54, (% for) $C_{27}H_{25}N_5O_3$ Calcd. C, 69.36; H, 5.39; N, 14.98; O, 10.27; found. C, 70.16; H, 5.42; N, 14.98; O, 10.30

Compound (3e): (Z)-N-(3-Bromo-4,5dimethoxybenzylidene)-4-chloro benzene-amine Green solid; M.P. 160^{o}C; Yield-68%; FT-IR (KBr): 3069 (w), 3059 (m), 1621 (s), 1575 (s), 1205 (m), 1013 (w), 740 (s) and 688 (m) cm^{-1} ^{1}H NMR (300 MHz, DMSO-d6) δ : 3.78 (s, 3H, OMe); 3.80 (s, 3H, OMe)7.30-7.66 (m, 6H, Ar-H) 11.71 (s, 1H, NH), 9.58 (s, 1H, CH). MS: 356; $C_{15}H_{13}BrClNO_2$; calcu, C, 50.85, H, 3.72, Br, 23.00, Cl, 10.11, N 4.00, O, 8.88, found; C, 50.82, H, 3.70, Br, 22.90, Cl, 10.12, N 3.99, O, 8.88.

CONCLUSION

This methodology is maintaining environmental friendly approach for the synthesis of benzylidine derivatives using $Ni(NO_3)_2.6H_2O$. The attractive features of this procedure are its good conversions, easy workup, and short reaction times, making it a useful practical method for the synthesis of Schiff bases. So reaction condition, we chose were the molar ratio of aldehyde and amine with 5% aqueous solution of $Ni(NO_3)_2.6H_2O$.

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