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MICROWAVE ASSISTED SYNTHESIS OF SCHIFF BASE LIGANDS UNDER SOLVENT FREE CONDITION – A GREEN APPROACH

E.Thamarai Selvi[1] and S.Mahalakshmi[2]

[1]Anna Adarsh College for Women, Department of Chemistry, Chennai-40, Tamilnadu, India.
[2] Pachaiyappas College, Department of Chemistry, Chennai-30, Tamilnadu, India.

ABSTRACT

Schiff bases are derived by the condensation of an amino compound with carbonyl compound. Heterocyclic Schiff base ligands have various applications which include antibacterial, antifungal, antiviral and antitumour activity. In the current work two Schiff base ligands have been synthesized from 4-aminoantipyrine, Thiophene-2-Carboxaldehyde / Pyrrole-2-carboxaldehyde both by the conventional method and microwave assisted method. The ligands are characterized by UV and FTIR and are screened for antibacterial activity.

Keywords: Schiff base, 4-aminoantipyrine, Microwave assisted synthesis.

INTRODUCTION

Schiff bases have been known since 1864 when Hugo Schiff reported the condensation of primary amines with carbonyl compounds [1]. The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R_1, where R and R_1 are alkyl, aryl, cyclo alkyl or heterocyclic groups.

The term "green chemistry" is defined as inventing, designing the chemical products and processes to reduce or to eliminate the use and generation of hazardous substances. In olden days, chemists thought that compounds react only in the liquid state or when dissolved [2]. This has made solvents common in chemical synthesis, however many compounds used as solvents were found to be environmentally harmful. By performing reactions without a solvent under microwave irradiation (MWI) [3] the problem associated with waste disposal of solvents has overcome. Coupling of MWI with the use of mineral-supported catalyzed reactions, under solvent-free conditions, provides clean chemical processes with the advantage of enhanced reaction rates, higher yields, greater selectivity, and greater ease of manipulation [4]. Recent years, usage of microwaves for carrying out chemical reactions has become a useful non-conventional energy source for performing organic synthesis [5]. This is supported by maximum number of synthesis performed using microwave [6-13]. In 1986 the rapid growth of microwave assisted procedures in organic synthesis was started and supported by pioneering papers by Gedye and co-workers [14] and Giguere and coworkers [15]. During the last two decades, the activity in this new technique has experienced exponential growth and has been extensively reviewed [16-20].

MATERIALS AND METHOD

All the reagents used for the synthesis 4-aminoantipyrine, Thiophene-2-carboxaldehyde, Pyrrole-2-carboxaldehyde were purchased from Merck and Himedia and were used as such. Melting points were determined in open capillary tubes in a 'Innco' electrical apparatus and are uncorrected .The UV-Visible spectra were recorded onSchimadzu UV spectrometer in the wavelength range 200 – 800 nm. IR spectra were recorded on Schimadzu FTIR 8400S spectrometer in the wavelength range 4000-400 cm^{-1} using KBr pellet. For microwave irradiation a Kenstar (OM-20ESP, 2450 MHz) domestic microwave oven was used.

Corresponding Author: - **E.Thamarai Selvi** Email: thamaraithirumaran@ymail.com

Antibacterial activity

Different concentration (10, 20 and 30 mg/ml) of the Schiff base ligands were tested for its antimicrobial strain such as *Staphylococcus aureus, Pseudomonas aeruginosa.* The bacterial cultures were grown in Mueller Hinton Agar and Mueller Hinton broth (Himedia) Lopez et al., (2001).

Antibacterial activity was measured using the standard method of diffusion disc plates on agar Erturk et al., (2006). 0.1ml of each culture of bacteria was spread on agar plate surfaces. For antibacterial assay all bacterial strains were grown in Mueller Hinton Broth Medium (Hi media) for 24 hours at 37°C and plated on Mueller Hinton Agar (Hi media) for agar diffusion experiments. Paper disc (6mm in diameter) were placed on the agar medium to load 20µl of different concentrations of Schiff base ligands. Inhibition diameters were measured after incubation for 24 - 48 hours at 37°C.

Synthesis of Schiff base ligands by conventional method

Synthesis of AAPTC ligand

An ethanolic solution (1 mmol, 0.2 g) of 4-aminoantipyrine was added to an ethanolic solution of Thiophene-2-carboxaldehyde (1 mmol, 0.1 g) and the solution was refluxed for 2-3 hours with vigorous stirring. The completion of the reaction was followed using TLC and it was allowed to crystallize at room temperature. After 24 hours a shining yellow precipitate was obtained which was washed several times with ethanol and was dried at room temperature. The sample was recrystallised using ethanol.

Synthesis of AAPPC ligand

An ethanolic solution (1 mmol, 0.2 g) of 4-aminoantipyrine was added to an ethanolic solution of Pyrrole-2-carboxaldehyde (1mmol, 0.095 g) and the solution was refluxed for 4-5 hours with vigorous stirring. The completion of the reaction was followed using TLC and it was allowed to crystallize at room temperature. After 24 hours a shining golden yellow precipitate was obtained which was washed several times with ethanol and was dried at room temperature. The sample was recrystallised using ethanol.

Microwave assisted Synthesis of Schiff base ligands

Synthesis of AAPTC ligand

4-aminoantipyrine (1 mmol, 0.2 g) and Thiophene-2-carboxaldehyde (1 mmol, 0.1 g) were ground well using mortar and pestle and were transferred in to the sample tube and irradiated in the microwave oven for 2 min. The completion of the reaction was monitored using TLC for every 30 sec. The sample was recrystallised using ethanol.

Synthesis of AAPPC ligand

4-aminoantipyrine (1 mmol, 0.2 g) and Pyrrole-2-carboxaldehyde (1 mmol, 0.095 g) were ground well using mortar and pestle and were transferred in to the sample tube and irradiated in the microwave oven for 2 min. The completion of the reaction was monitored using TLC for every 30 sec. The sample was recrystallised using ethanol.

RESULTS AND DISCUSSION

Physical Data

A comparative account of the physical data of the two ligands synthesized by conventional method and microwave method were given in Table.1. The reaction carried out using conventional method required about 3– 5 hours, while microwave irradiation method required only 2 min.

Spectral studies

The IR and UV spectral details of the ligands synthesized by conventional and microwave method were given in Table 2 and Table 3.

The IR Spectrum of the ligands showed bands in the region 1586-1643 which proves the formation of azomethine group (**ν (C=N)).**

Antibacterial activity

The susceptibility of certain antimicrobial strains towards the Schiff base ligands was judged by measuring the size of the inhibition diameter.

The result shown in Table 4 indicates that the Schiff base ligands show good activity against *Pseudomonas aeuroginosa* and *Staphylococcus aureus*.

Table 1. Physical data

Schiff base	Empirical formula	Conventional				Microwave			
		Reaction Time (in hours)	colour	Yield %	M.P	Reaction Time (in min)	colour	Yield %	M.P
AAPTC	$C_{16}H_{15}N_3OS$	3	Glittering yellow	75	170-171	2	yellow	98	170
AAPPC	$C_{16}H_{15}N_4O$	5	Glittering golden yellow	70	195-196	2	Golden yellow	95	195

Table 2. IR spectral data

Schiff base	Conventional method		Microwave method	
	ν cm^{-1} (C=N)	ν cm^{-1} (aromatic stretching)	ν cm^{-1} (C=N)	ν cm^{-1} (aromatic stretching)
AAPTC	1641	1562 1575 1497 1486	1643	1537 1499 1415
AAPPC	1587	1431 1333	1586	1433 1335

Table 3. UV spectral data

Schiff base	Conventional method			Microwave method		
	λ_{max} (nm)	Absorbance	ε_{max}	λ_{max} (nm)	Absorbance	ε_{max}
AAPTC	348	2.337	233.7	351	2.671	267.1
AAPPC	344	2.904	290.4	345	3.118	311.8

Table 4. Antibacterial activity

Compound	*Pseudomonas aeruginosa*			*Staphylococcus aureus*		
	10mg/ml	20mg/ml	30mg/ml	10mg/ml	20mg/ml	30mg/ml
AAPTC (conventional)	10	15	20	-	13	15
AAPTC (microwave)	10	15	20	-	13	15
AAPPC (conventional)	11	20	23	-	10	15
AAPPC (microwave)	11	20	23	-	10	15

(Zone of inhibition in mm): no activity (0.0), very weak activity (< 7 mm), weak activity (7–10), moderate activity (11–15 mm), strong activity (> 15 mm).

CONCLUSION

In this work we have reported a novel method for the synthesis of Schiff bases using microwave irradiation which offers significant improvements over existing conventional procedures. From the data of antimicrobial activity, it could be observed that the ligands showed moderate to strong activity against the bacterial strains. Microwave assisted synthesis could be used as an important tool for the synthesis of various medicinally important agents with short reaction times, excellent yields and without formation of undesirable side products.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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