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RESEARCH ARTICLE

Microwave Assisted Synthesis of Naphthaoxazole Using PEG-SO3H as Heterogeneous Catalyst and its Antimicrobial Activity

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ABSTRACT

Heterocyclic moieties are abundant in environment & are of great importance to life because their constitutional subunits exist in a lot of natural compounds such as hormones, vitamins and antibiotics; therefore, they have involved significant awareness in the design of biologically potency molecules & advanced organic chemistry. Organic chemistry involving number of synthesis in which heterocyclic compound may synthesized using several catalysts may include both homogeneous and heterogeneous type. In this context we have developed environment benign novel protocol for synthesis of various substituted naphthaoxazole was prepared using aromatic aldehydes and 3-amino-2-naphthol by Microwave heating method. This protocol of synthesis of PEG-SO3H catalyzed naphthaoxazole using condensation reaction between 3-amino-2-naphthol and various aldehydes under ethanol as solvent using microwave heating method. A series of compounds were prepared and characterized by 1HNMR, 13CNMR, IR and Mass spectroscopy. Prepared products were checked for their antimicrobial activity against gram +ve & gram –ve bacteria.

KEYWORDS

3-amino-2-naphthol, PEG-SO3H, Antimicrobial study, Microwave, naphthaoxazole, Spectral Characterization

INTRODUCTION

Heterocyclic compounds consist of cyclic structures in which one or more of the ring atoms are of elements other than carbon. The common hetero atoms are nitrogen, oxygen and sulphur. About a third of known organic compounds are heterocycles. They can be divided into alicyclic and aromatic compounds, which possess five or six member rings. The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It has seen unparalleled progress owing to their wide natural occurrence, specific chemical reactivity and widespread utility in the field of therapeutics.

Benzo fused azoles are an important class of compounds. They provide a common heterocyclic scaffold in biologically active and medicinally significant compounds **[1-6]**.

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Benzoxazoles are found in a variety of natural products **[7]** and are important targets in drug discovery **[8]**. They also find applications in material science as photochromic agents and laser dyes **[9]**.

There has been a recent surge in the development of new benzoxazole syntheses because of their potential uses as cytotoxic agents **[10-12]**, cathepsin S inhibitors **[13]**, HIV reverse transcriptase inhibitors **[14]**, estrogen receptor agonists **[15]**, selective peroxisome proliferator activated receptor antagonists, anticancer agents **[16]** and orexin-1 receptor antagonists **[17]**. They have also found application as herbicides and as fluorescent whitening agent dyes **[18]**. 2-Arylbenzoxazoles are an important group of target molecules by virtue of their special photo physical properties **[19-21]** and biological activities, including antitumor, antimicrobial, and antiviral properties **[22]**. It has also been reported that arylbenzoxazole-containing amino acids have high fluorescence quantum yields and can be engineered into convenient fluorescent probes **[23-25]**. Recently, it has been reported that 2-arylbenzoxazoles are novel cholesteryl ester transfer protein inhibitors **[26]**, and some 2-arylbenzoxazoles are highly selective amyloidogenesis inhibitors **[27]**.

Our aim to developed novel protocol for synthesis of Naphthaoxazole using green heterogeneous catalyst PEG-SO_3H under Microwave Irradiation in shorter reaction time with good yield and all prepared compounds were checked for biological activities.

1.2 Materials and Methods

1.2.1 Chemicals and Reagents

Laboratory grade chemicals used are 3-amino-2-naphthol, Aldehydes, PEG-6000, Sulfonicacid, methylenedichloride, ether and alcohol were purchased from Samir Tech Chem. Pvt. Ltd., Vadodara, India.

1.2.2 Instruments

Bruker Avance-400 instrument was used for Proton NMR study and 100MHZ frequency instrument was used for ^{13}C NMR. Parts per million unit was used to expressed chemical shift value. ABB Bomem Inc. FT-IR 3000 Spectrophotometer was used for Infrared Spectral study. Data obtained was expressed in cm^{-1} unit. Shimadzu LCMS-2010 was used for MASS spectral analysis. Perkin Elmer-2400 Series II CHNS/O Elemental Analyzer was used for Composition measurement.

1.2.3 Synthesis of PEG-SO_3H catalyst

A catalyst was prepared by report method **(Hasaninejad et al., 2011)** at $0^{\circ}C$, 10 mmol Chlorosulfonic acid (1.16 g) was mixed up with PEG-6000 solution (6 g, 1 mmol) in 10ml CH_2Cl_2. Shake the mass at room temperature for few minutes followed by allow to stand overnight and concentrated under vaccum. Followed by addition of 60ml ether & precipitates was obtained are filter and washed

with 30 ml of ether three times to afford the PEG-SO_3H.

1.2.4 Methods for preparation of compounds K15-K28

Take **1 mmol benzaldehyde** in 250ml round bottom flask, add 1 mmol amount of 3-amino-2-naphthol, 5 mmol% of PEG-SO_3H with respect to 3-amino-2-naphthol and 5 ml ethanol as the solvent, reflux the mixture under microwave with optimize power level 240Watt for **3 minutes**. TLC (Thin layer Chromatography) is used for monitoring reaction. Once reaction is over, remove solvent by evaporation with proper care & separated the finest product obtained. This has been confirmed using spectroscopic techniques and Melting point determination as well as elemental analysis.

Table 1 The characteristic data showing the synthesis of Naphthaoxazole

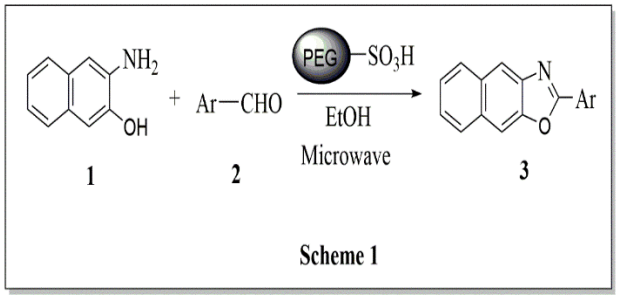
Compound Code	Ar	Microwave Irradiation 240 W	
		Reaction Time[a] (min)	Yield[b] (%)
K-15	C_6H_5-	3	83
K-16	4-CH_3-C_6H_4-	3	73
K-17	4-Cl-C_6H_4-	3	88
K-18	2-Cl-C_6H_4-	3	86
K-19	4-NO_2-C_6H_4-	3	88
K-20	2-NO_2-C_6H_4-	3	86
K-21	3-NO_2-C_6H_4-	3	88
K-22	2-C_4H_3O-	3	83
K-23	4-OCH_3-C_6H_4-	4	72
K-24	2-OH-C_6H_4-	3.5	72
K-25	3-OH-C_6H_4-	3.5	78
K-26	4-OH-C_6H_4-	3.5	80
K-27	2-COOH-C_6H_4-	3	80
K-28	4-OH-3-OCH_3-C_6H_3-	3.5	73

[a]TLC method used for completion of reaction; [b]Isolated yields.

1.3 Result and Discussion

1.3.1 Reaction Scheme

3-amino-2-naphthol (0.01 mole) and benzadehyde (0.01 mole) react by using catalytically amount of 5 mmol % PEG-SO_3H with respected to weight of 3-amino-2-naphthol under 10ml ethanol as solvent using Microwave to affords Naphthaoxazole (**Scheme 1**).



Scheme 1

1.3.2 Optimization of reaction condition

Model reaction was carried out for optimization by taking 0.01mol benzaldehyde 1a and 0.0105mol 3-amino-2-naphthol 2 by convectional energy source to produced compound 2-aryl substituted naphthaoxazoles K-15 (Scheme 1). PEG-SO3H a heterogeneous catalyst was used in the ratio of mmole % with respect to 3-amino-2-naphthol. The reaction optimization was done in terms of reaction duration and amount of catalyst required to produced maximum yield. Reaction was monitored using thin layer chromatography. The resultant data obtained are shown in Table 2.

Table 2 Effect of different catalyst on the condensation of 3-amino-2-naphthol and benzaldehydes in ethanol under microwave

Entry	mmol% PEG-SO_3H	Under Microwave.	
		Time[a] (min)	Yields[b] (%)
	1	2	80
	2	2	80
	3	2	80
	4	3	78
	5	**3**	**83**
	6	3	78
	7	3	78
	8		

[a] Reaction was monitored by TLC, [b] Isolated yields.

The same model reaction was optimized under microwave irradiation by taking different amount of catalyst, it was found that best result again obtained by taking 5mmol% amount of catalyst. The microwave power level was also optimized by taking 5mmol% amount of **PEG-SO_3H** with respect to diamine. It was found that best result was obtained at power level 240 Watt. At this power level reaction was completed in 3minutes with 83% yield of product as shown in Table 3.

Table 3 Data representing the optimization for synthesis of Naphthaoxazole by the assistance of MWI technique. [a, b]

Power Levels in Watt	Reaction Time (min)[a]	% Isolated Yield[b]
140	4	63
210	4	78
240	**3**	**83**
280	3	73
350	3.5	73

[a]Reaction was monitored by TLC; [b]Isolated yields.

1.4 Antimicrobial Activity of Compounds K15-K28

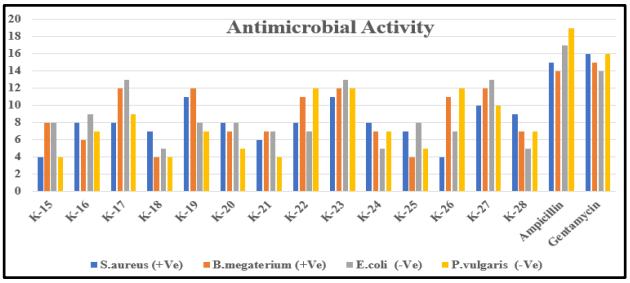


Figure-1 Antimicrobial activity of Compounds K-15 to K-28

From the above **Figure-1** it shown that following are the results with maximum and minimum zone of restriction vale.

(a) Against Staphylococcus aureus:

Compounds **K-19** and **K-23** shows maximum potency with zone of restriction-11.0 m.m. whereas minimum potency was shown by compounds **K-15** and **K-26** with zone of restriction 4.0 m.m.

(b) Against Bacillus megaterium:

Compounds **K-17, K-19, K-23** and **K-27** shows maximum potency with zone of restriction-12.0 m.m. whereas minimum potency was shown by compounds **K-18** and **K-25** with zone of restriction 4.0 m.m.

(c) Against Escherichia coli:

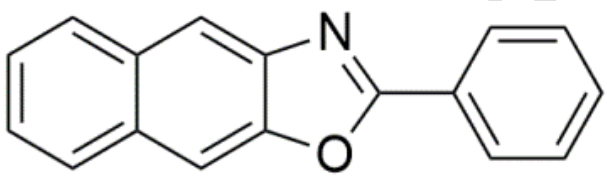
Compounds **K-17, K-23** and **K-26** shows maximum potency with zone of restriction-13.0 m.m. whereas minimum potency was shown by compounds **K-18, K-24** and **K-28** with zone of restriction 5.0 m.m.

(d) Against Proteus vulgaris:

Compounds **K-22, K-23** and **K-26** shows maximum potency with zone of restriction-12.0 m.m. whereas minimum potency was shown by compounds **K-15, K-18** and **K-21** with zone of restriction 4.0 m.m.

1.5 Characterization

K15 as a sample compound was taken for characterization. Following Spectroscopic results were obtained and its well agreement with proposed structure of 2-phenylnaphtho[2,3-d] oxazole **(K-15).**

Compound K-15  **2-phenylnaphtho[2,3-d]oxazole**	
Molecular Formula	$C_{17}H_{11}NO$
Molecular Weight ($g \cdot mol^{-1}$)	245.10
Melting Point (°C)	165
^{1}H NMR (DMSO, 400 MHz): δ ppm 7.3 (2H, m), 7.6-7.4 (3H, m), 7.7 (1H, m), 7.8 (1H, m), 8.3 (4H, m).	
^{13}C NMR (DMSO, 100 MHz): δ ppm 110.6 119.9, 124.5, 125.1, 127.3, 127.5, 128.9, 131.5, 142.2, 150.8, 156.1, 158.0, 163.0.	
DEPT-135: Up peaks: 163.0, 158.0, 156.1, 150.8, 142.2, 131.5 **Down peaks:** 128.9, 127.5, 127.3, 125.1, 124.5, 119.9, 110.6	
IR (KBr) cm-1: 3047 (w), 1454, 1404, 1260, 968, 750 cm^{-1}	
LC-MS: 245.10	
% C, H, N Analysis: Calculated: C, 83.25; H, 4.52; N, 5.71 Observed: C, 83.34; H, 4.60; N, 5.73	

Conclusion

We have reported environment benign novel protocol for synthesis of various naphthaoxazole using 3-amino-2-naphthol and different aromatic aldehyde under microwave heating method. Reaction product was obtained in shorter reaction time with good yield of product. Prepared compounds were also tested for antimicrobial activities and it was found that K-15, K-17 to K-22 shows good activity.

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