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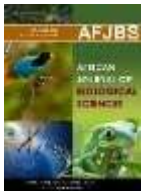

One Pot Multi-Component Preparation Of Highly Functionalized Bio-Active Oxazine Derivatives By Using Silicotungustic Acid Catalyst Under Microwave Irradiation.

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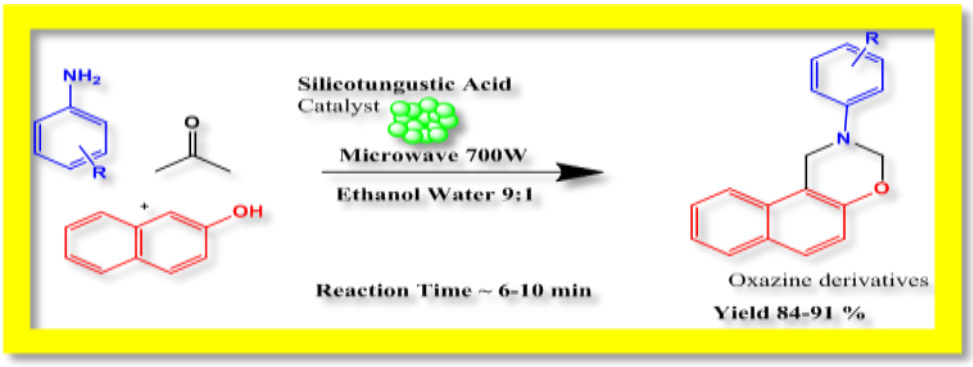
Abstract

One pot multi-component synthesis of heterocyclic bioactive Oxazine derivatives has been demonstrated by using catalyst Silicotungustic acid under microwave irradiation. The Oxazine derivatives are prepared using ethanol and water solvent in 9:1 ratio. The reactions are very fast and high yielding (~ 84-92 % product yield) within few minutes. The catalyst is easily isolated at the end of the reaction by simple filtration technique. The catalytic activity remains unchanged till the 7th cycle. The key advantage of this reaction is green reaction media aq. ethanol and rapid reaction time reusable catalyst and eco-friendly route using microwave irradiation.

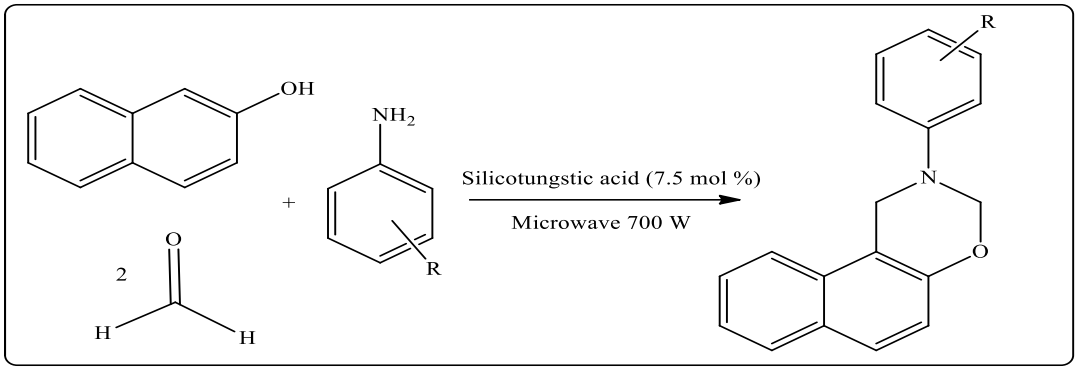
Keywords: Substituted Aniline, β-Naphthol, Formalin, Silicotungsticacid, Microwave irradiation etc.

Graphical Absrtract



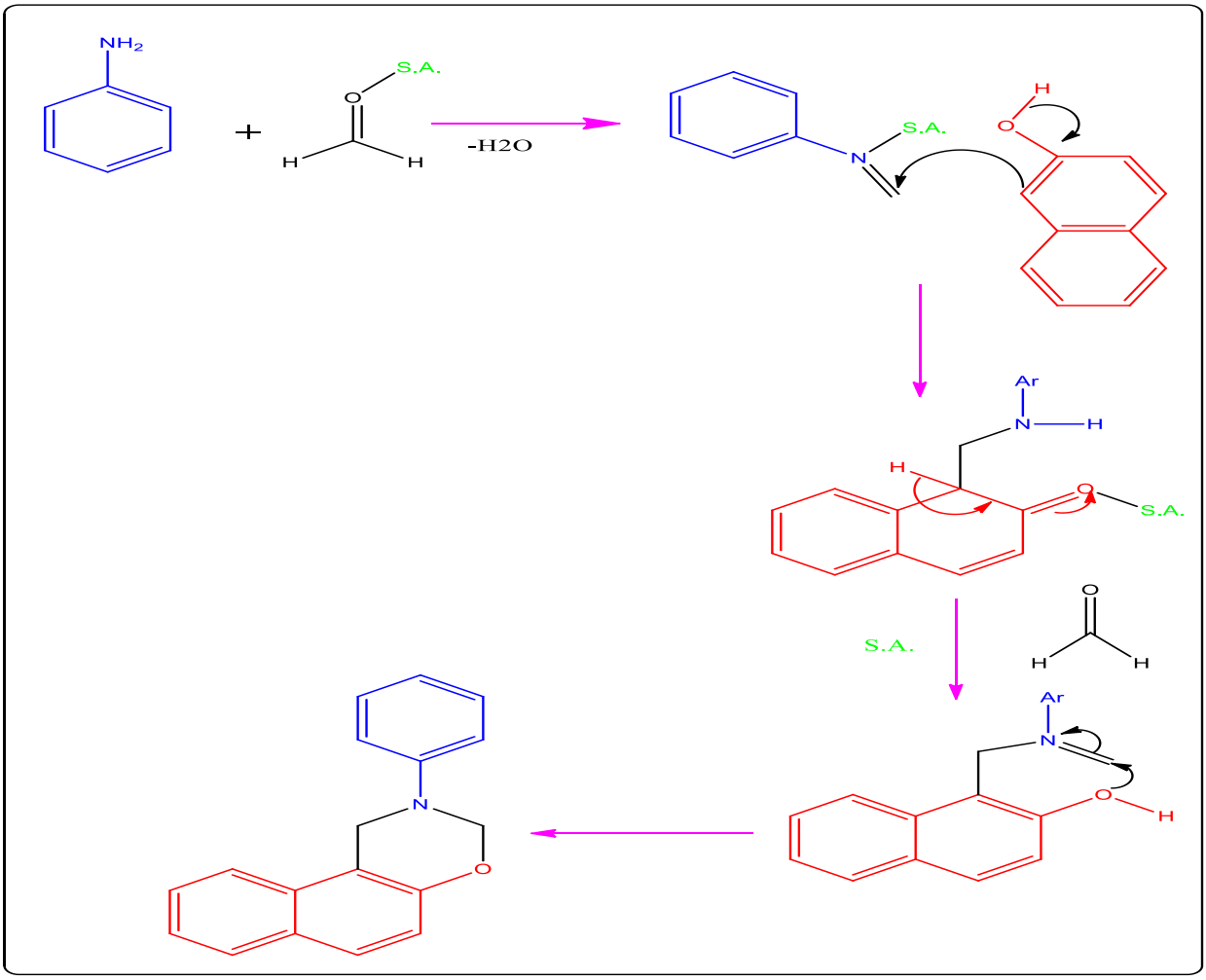
Introduction:

Heterocyclic chemistry research play significant role inthe organic chemistry. Many bioactive molecules containing the oxazine core play an important role in the drug invention process and exhibit a wide range of activities [1-2]. Studies on 1,3-oxazine heterocyclic compounds have shown that they have many toxic properties such as antibacterial, antiviral, antibacterial, antifungal, and anti-inflammatory [3-4]. These compounds have received particular attention since the invention of the non-nucleoside turn around transcriptase inhibitor trifluoromethyl-1, 3-oxazin-2-one, which has sky-scraping activity against many HIV-1 strain mutants[5]. Additionally, naphthoxazine derivatives have been shown to show potential in the action of Parkinson's disease [6, 7]. 2,3-dihydro 1-*H*-naphtho[1,2-e] 3,4-dihydro 2-*H*-naphtho[2,1-e] [1,3] Synthesis of Oxazineinvolve one-pot condensation Cyclization of naphthols, formaldehyde and primary amines. a variety of methods have been report in the literature, including BF_3-SiO_2 [8], thiamine hydrochloride (VB_1) [9], ammonium metavanadate [10], ILs [11] and alum [12].Solid phase synthesis has attracted great attention recently. This method has the reward of high efficiency, high selectivity, simple separation and purification, and small reaction [13]. Not only are they environmentally friendly, they are also favorable because toxic waste can be reduced or eliminated. The collision-type reaction phase was first used in the Grignard reaction [14], Reformatsky reaction [15], aldol condensation [16], Dieckmann condensation [17-18], Knoevenagel condensation reduction [19-20] and extra vaccines. [1,3] oxazine derivatives by means of 2-naphthol, formalin, and various anilines as substrates in the existence of silicotungstic acid in the microwave. To the most excellent of our knowledge, there is no study on the one-pot synthesis of 3,4-dihydro 3-substituted 2H-naphtho[2,1-e][1,3] oxazine by usingsilicotungstic acid.



Scheme:Synthesis of 2,3-Dihydro- 2-Phenyl -1*H*-Naphtho[1,2e] [1,3] Oxazine

Mechanism of the Reaction



II. RESULT & DISCUSSION

Here, we would like to account the preparation of 3, 4-dihydro-3 substituted 2*H*-naphtho[2,1-e][1,3] derivative of Oxazine supported bysilicotungstic acid (Scheme I). We used 2 naphthol (1 mmol), formaldehyde (2 mmol), and aryl amine (1 mmol) at room temperature as reaction standards. Optimize the reaction to evaluate the effectiveness of silicotungstic acid as a catalyst in the reaction (Table-1). The results showed so as to the silicotungstic acid catalyst produced the desired product in 92 % yield in 7 min; this is a good figure (Table-1, Sr. No. 4).

Table 1: Effect of catalyst conc.[a]

Sr. No.	Catalyst Conc. (mol %)	Yield (%)[b]
1	2.5	65
2	5	75
3	7.5	92
4	10	92
[a]Reactionconditions :2 napthol(1 mmol), formalin(2 mmol), aryl amine(1 mmol), silicotungstic acid (7.5 mol %), Microwave 700W. [b]Isolated yield.		

Examine the catalyst loading concentration of the model reaction, The process was optimized using dissimilar molar amounts of silicotungstic acid (7.5 mol) in microwave 700W. A excellent yield of product 4h was experimental when 7.5 mol% catalyst was used. From these outcome, it can be seen so as to the catalyst concentration plays an important role in improving the results to a superior extent. Additionally, it was observed that there was no significant change in product yield for catalysts larger than 7.5 mol%.To evaluate the solvent effect, various solvents such as tetrahydrofuran, acetonitrile, dichloromethane, water, water: ethanol (1:1), methyl alcohol, ethyl alcohol and H_2O: ethyl alcohol (1:9) was used for the model reactions. The preferred product was obtained in 35, 64 55, 58, 66, 84, 88and 92 % yields correspondingly after respective time at room temperature conditions. Ethyl alcohol: Water: (1:9) be notable as the solvent of selection amongst the solvents experienced. Because of the fastest conversion & desired product obtained higher yield (Table 2, Sr. No. 8), whereas the product formed in lesser yieldin longer time by using varies ratio of water & ethyl alcohol solvents.

Table 2: Screening of solvents

Sr.No.	Solvent	Yield (%)
1	Tetrahydrofuran	35
2	Acetonitrile	64
3	Dichloromethane	55
4	Water	58
5	Methyl alcohol	66
6	Ethyl alcohol	84
7	Water: ethanol (1:1)	88
8	Water: Ethyl alcohol (1:9)	92

For this model, we performed electron-donating and electron-withdrawing experiments of other amines and obtained the corresponding product [1,3] Oxazine derivatives in positive reactions. In most cases the yields were good to very good, as shown in Table-3.

Table - 3: Preparation of Oxazine derivative by using Silicotungstic acid.

	Aromatic amine	Time (min)	Yield [b](%)	M. P °C
1	$C_6H_5-NH_2$	6	91	46-48
2	$2-CH_3-C_6H_4-NH_2$	8	89	58-60
3	$2-NO_2-C_6H_4-NH_2$	10	88	108-110

4	3-CH_3-C_6H_4-NH_2	9	90	70-74
5	2-OCH_3-C_6H_4-NH_2	6	91	74-78
6	3-NO_2- C_6H_4-NH_2	9	89	133-134
7	4-CH_3-C_6H_4-NH_2	7	91	88-89
8	4-OCH_3-C_6H_4-NH_2	5	92	76-80
9	4-NO_2- C_6H_4-NH_2	8	83	169-170
10	4-Br- C_6H_4-NH_2	8	87	115-116
11	4-OC_2H_5- C_6H_4-NH_2	9	90	135-138
12	4-F- C_6H_4-NH_2	6	86	69-71

III. EXPERIMENTAL

Method & Material:

All the chemical compound used in this method were purchase from Merck without Purification. M. P. had been determined in an open capillary tube and are not corrected. The developments of the reactions were observed by TLC. ^{1}H NMR spectrum reported at 400 MHz with TMS as internal standard and dimethylsulfoxide DMSO as solvent on Bruker NMR spectrometer, Fourier transform infrared (IR) spectroscopy were obtained as KBr discs on a Bruker FT-IR / FT-FIR spectrometer and mass spectra on LCMS Water's Synapt-XS Maldi TOF HDMS spectrometer.

General Procedure for the Preparation of Oxazine derivative:

A mixture of β-naphthol (1 mmol),formalin (2 mmol), aryl amine (1 mmol), silicotungstic acid (7.5 mol%) and 7ml 90% aq. ethanol as a solvent. As indicated by TLC, irradiate 50 ml of ethanol in RBF with microwaves for the appropriate time in a 700 W microwave oven for 6-10 min (continue irradiation for 30-40 s with cooling time). After cooling, the reaction mixture is poured on top of crushed ice. The crude product is filtered, dried up and crystallized in ethyl alcohol solvent.

IV. CONCLUSION

We have developed ansuperficial, green route for the preparation of Oxazine derivative involving starting material 2-napthol, formalin and aromatic amine in presence of Silicotungstic acid (7.5 mol%) of catalyst under microwave 700W irradiation generate excellent yield. application microwave in the present synthesis ecological process require less reaction time, avoidance of hazardous chemicals and non conventional process afford high Yield.

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VI.CONFLICTS OF INTEREST

The Author declares that there are no conflicts to declare.

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