



Ammonium metavanadate: a mild and efficient catalyst for the synthesis of 2, 3-dihydro-2-phenyl-1H-naphtho-[1, 2-e] [1,3]oxazine derivatives

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ABSTRACT

An efficient and simplified protocol for boric acid catalyzed solvent-free synthesis of β -enaminones derivatives under microwave irradiation is described. The remarkable advantages offered by this method are inexpensive and readily available catalyst, simple procedure, faster reactions and high yield of products. © 2015 Trade Science Inc. - INDIA

KEYWORDS

Ammonium metavanadate;
Mild catalysts;
[1,3]oxazine.

INTRODUCTION

Heterocyclic compounds having wide applicability and plays essential role for living systems. In the last few decades, among a large variety of heterocyclic compounds, 1,3-oxazine containing moiety possess wide synthetic utility as a useful intermediate for the variety of functional group interconversions such as for the synthesis of various ketones^[1] trans β -inoglidene acetaldehyde^[2] carboxylic acids, trans olefins^[3]. Recently, 1,3-oxazine ring system has been used for the photo induced opening and thermal closing of the oxazine ring^[4] Furthermore, they can be used as intermediates in the synthesis of N-substituted amino alcohols (Betti base) or in enantioselective synthesis of chiral amines^[5].

In recent years, 1,3-oxazine heterocycles has been evaluated for the varied biological properties such as analgesic, anticonvulsant, antitubercular, antibacterial, anticancer activity^[6] and shows high

activity against a variety of HIV-1 mutant strain^[7] In addition, naphthoxazine derivatives have exhibited therapeutic potential for the treatment of Parkinson's disease^[8]. The tautomeric character of 1,3-*O,N*-heterocycles offer a great number of synthetic possibilities^[9]

Generally, 1,3-oxazine derivatives have been reported in few classical methods such as by the condensation of 2-naphthol, aromatic aldehydes in the presence of dry methanolic ammonia,^[10] uncatalyzed and solvent-free synthesis using 2-naphthaldehyde and ammonium acetate as a nitrogen source,^[11] using nitriles and amino alcohols in the presence of Cu(OAc)₂, ZnCl₂ as a catalyst,^[12] using *N*-acyl-4-acyloxy- β -lactones under basic condition^[13], intramolecular hydroamination of trichloro acetamide in the presence of Au(I) complex^[14], cycloaddition reaction using 2-azadienes with alkynes^[15] and Intramolecular cyclisation of N-thioacyl-1,3-aminoalcohols with Bu₄NF and EtI^[16]

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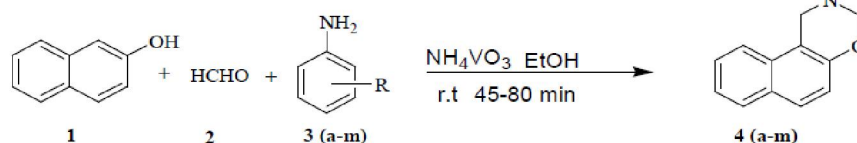
More recently by microwave irradiation and under classical conditions using *p*-TsCl 4DMAP/CH₂Cl₂ under reflux condition from 3-amino-1-propanol in two steps has been reported^[17] But on the titled molecule there have only been a few reports from formaldehyde, 2-naphthol and aromatic amines^[18]. However, these methods have their own merit while some of these are plagued by the limitation of prolonged reaction time, exotic reaction conditions and lower yields. Hence, the development of a new method for the synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine derivatives would be highly desirable.

The art of performing efficient chemical transformation coupling three or more components in a single operation by a catalytic process avoiding stoichiometric toxic reagents large amounts of solvents and expensive purification techniques represents a fundamental target of the modern organic synthesis^[19].

Hence the search continues for a better catalyst in the synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine in terms of operational simplicity and economic viability. Herein we report the use of ammonium metavanadate (NH₄VO₃) as a water soluble, inorganic acid^[20] that meets the demand for an economic catalyst. It is employed similar to vanadium pentoxide^[21] as a catalyst in oxidation reactions with other cocatalysts^[22]. It is a reagent used in analytical chemistry, the photographic industry, and the textile industry^[21]. This is the first report of utilizing ammonium metavanadate as a catalyst for the synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine.

EXPERIMENTAL

Apparatus and reagents



Scheme 1

All aldehydes were obtained from freshly opened container and used without further purification with the exception of benzaldehyde and 2-furaldehyde which were distilled prior to use melting point was determined in open capillary tubes and is uncorrected. IR spectra were recorded on Perkin Elmer FTIR spectrophotometer in KBr disc, ¹H NMR spectra were recorded on variant 300 MHz spectrophotometer meter in CDCl₃ using TMS as internal standard. The chemical shifts have been expressed in δ-ppm scale the melting points and other data were recorded in TABLE 3 General procedure for Synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine derivative

General procedure for the synthesis 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]

Oxazine derivatives

A mixture of formalin (1 mmol), aromatic amine (1 mmol), 2-naphthol and ammonium metavanadate (10 mol %) in ethanol (5 ml) was stirred at room temperature for 45-120 min. The progress of the reaction was monitored by TLC. After completion of reaction conversion, the reaction mixture was poured on crushed ice. The obtained crude solid product was filtered, dried and crystallized from ethanol. Our search for an efficient catalyst and the best experimental reaction conditions in the preparation of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine, we have determined that the reaction of β-naphthol, formaldehyde and aniline 3a in ethanol at room temperature is the standard model reaction.

RESULT AND DISCUSSION

In continuation of our research devoted novel synthetic methodologies^[23], herein, we report a simple, efficient, and rapid method for the synthesis

of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine derivatives catalyzed by ammonium metavanadate (Scheme 1).

The reaction of an aniline 3a as a representative aromatic amine, 2-naphthol and formalin in the presence of ammonium metavanadate has been considered as a standard model reaction for the optimization of reaction condition.

To evaluate the effect of solvent, we have screened different solvents such as water, water:

ethanol (1:1), tetrahydrofuran, acetonitrile, dichloromethane, methanol and ethanol at room temperature. Ethanol stand out as the solvent of choice among the solvents tested because of the rapid conversion and excellent yield (93%) of desired product, where as the product formed in lower yields (00-70 %) by using other solvents (TABLE 1, Entry 1-5).

To determine the optimum concentration of catalyst, we have investigated the model reaction at 5,

TABLE 1 : Screening of solvents^a

Entry	Solvent	Yield ^b (%)
1	Water ^a	-
2	Water :ethanol (1:1)	-
3	Tetrahydrofuran	35
4	Acetonitrile	45
5	Dichloromethane	54
6	Methanol	70
7	Ethanol	93

^aReaction conditions: 1 (1 mmol), 2 (2 mmol), 3a (1 mmol), ammonium metavanadate ^bIsolated yields.

TABLE 2 : Effect of concentration of ammonium metavanadate^a

Entry	Concentration (mol %)	Yield ^b (%)
1	5	60
2	7.5	77
3	10	93
4	12.5	93

^aReaction conditions: 1 (1 mmol), 2a (1 mmol), 3 (3 mmol) in ethanol at room temperature. ^bIsolated yields.

TABLE 3 : NH₄VO₃ catalyzed synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine

Entry	Comp-ound	Ar-NH ₂	Time (min)	Yield (%)	M.P. (°C)	
					Found	Literatue
1	4a	C ₆ H ₅	60	93	48-50	49-51
2	4b	2CH ₃ - C ₆ H ₄	55	94	55-57	56-58
3	4c	3CH ₃ - C ₆ H ₄	65	90	70-72	70-72
4	4d	4CH ₃ - C ₆ H ₄	45	92	87-89	88-90
5	4e	2NO ₂ - C ₆ H ₄	85	90	107-109	110-112
6	4f	3NO ₂ - C ₆ H ₄	70	91	127-129	129-131
7	4g	4NO ₂ - C ₆ H ₄	55	88	164-166	165-167
8	4h	4Br- C ₆ H ₄	70	91	112-114	115-117
9	4i	2,4,6(Br) ₃ - C ₆ H ₂	80	75	95-97	96-98
10	4j	3OCH ₃ -C ₆ H ₄	65	89	65-67	66-68
11	4k	4OCH ₃ -C ₆ H ₄	60	74	79-81	78-80
12	4l	2OC ₂ H ₅ -C ₆ H ₄	65	89	100-101	100-102
13	4m	4F-C ₆ H ₄	75	90	135-136	135-137

^aReaction conditions: 1 (1 mmol), 2 (2 mmol), 3 (1mmol), NH₄VO₃ (10 mol%) in ethanol at room temperature. ^bIsolated yields.

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7.5, 10 and 12.5 mol% of ammonium metavanadate in ethanol at room temperature. The product was obtained in 82, 88, 93 and 93 % yield respectively. This indicates that the use of 10 mol% of ammonium metavanadate is sufficient to promote the reaction forward (TABLE 2)

To study the generality of this process, variety of examples were illustrated for the synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine and results are summarized in TABLE 3. The reaction is compatible for various substituents such as -CH₃, -OCH₃, -OH, -Br, -NO₂ and -Cl. The formation of desired product has been confirmed by ¹H NMR and IR spectroscopic analysis technique and compared with the corresponding literature data.

Spectral data of the the principal products:

2,3-dihydro-2-(4-methoxyphenyl)-1*H*-naphtho[1,2-*e*][1,3]oxazine (4k): ¹H NMR (DMSO) δ ppm 3.6 (s, 3H, Ar-OCH₃), 4.8 (s, 2H, N-CH₂), 5.4 (s, 2H, O-CH₂-N), 6.7-7.8 (m, 10H, Ar-H). MS m/z 292 (M⁺).

CONCLUSION

In conclusion, we have described a general and highly efficient procedure for the preparation of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine derivatives using commercially available inexpensive ammonium metavanadate in ethanol. The remarkable advantage of this protocol is mild reaction conditions, excellent yields of product, operational and experimental simplicity. We believe that, this methodology will be a valuable addition to the existing methods of the synthesis of 2,3-dihydro-2-phenyl-1*H*-naphtho-[1,2-*e*] [1,3]oxazine.

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