

Heterocyclic Letters Vol. 13/ No.1/105-113/November -January/2023 ISSN : (print) 2231–3087 / (online) 2230-9632 CODEN: HLEEAI <u>http://heteroletters.org</u>

"SILICA SUPPORTED PHOSPHOTUNGSTIC ACID AS GREEN HETEROGENEOUS CATALYST FOR ONE POT SYNTHESIS OF 1, 2-DIHYDRO-1-ARYLNAPHTHO [1, 2-E] [1, 3] OXAZINE-3-ONES"

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ABSTRACT

An efficient green route for the synthesis of 1, 2-dihydro-1-arylnaphtho [1, 2-e][1, 3]oxazine-3-ones derivatives, applying a facile and one-pot condensation reaction of 2-naphthol, aromatic aldehyde and urea in the presence of silica supported phosphotungstic acid under solvent-free conditions has been developed. The present procedure offers advantages such as short reaction time, clean reaction, simple workup, recovery and reusability of the catalyst.

KEYWORDS: Multi-component, heterogeneous catalyst, $H_3PW_{12}O_{40}/SiO_2$, Naphthoxazine-3-one, One-pot.

INTRODUCTION

Great research efforts have recently been devoted to studies with the aim of finding suitable heterogeneous alternatives to replace homogeneous catalystsⁱ. In most cases, heterogeneous catalysts possess comparable catalytic activities but their handling proved to be simpler. Solid supported reagents are unique acid catalysts that have become popular over the last two decades. The activity and selectivity of a reagent diffused on the surface of a support is amended as the effective surface area of the reagent is increased multifold and thus they more effective than the individual reagentsⁱⁱ. Among various solid supports, silica is usually preferred since it displays many advantageous properties such as high surface area, excellent stability (thermal and chemical), good accessibility and organic groups can be robustly anchored to the surface; to provide catalytic centers^{iii-v}.

Oxazinone, benzoxazinone and their derivatives are an important class of heterocyclic compounds, because many of these derivatives display biological activities, such as HIV-1 reverse transcriptase inhibitors^{vi}. Naphthalene-condensed 1,3-oxazin-3-one have been reported to act as antibacterial agents^{vii}. This class of compounds has also been used as precursors in the preparation of phosphinic ligands for asymmetric catalysis^{viii}. Since many of these heterocyclic

systems exhibit biological activities such as anti-inflammatory, antiulcer, antipyretic, antihypertensive and antifungal, these derivatives have become an integral part of pharmacologically important heterocyclic compounds^{ix-xiii}. Thus far, only few reports for the synthesis of naphthalene-condensed oxazinone derivatives have been reported in the literature. First time, Cope and Holly synthesized aromatic oxazines through the mannich reactions from phenols, formaldehyde and amines^{xiv}. Many naphthoxazines and benzoxazines were synthesized by Burke and co-workers^{xv-xxiii}. Recently, the preparation of naphthoxazinone derivatives using various catalyst such as TMSCl^{xxiv}, ZnO NPs^{xxv}, phosphomolybdic acid^{xxvi}, HClO₄/ SiO₂^{xxvii}, [bmim]Br^{xxviii}, CH₃SO₃H^{xxix}, P-TSA^{xxx}.

In this article, we present a one-pot, three-component method for the preparation of 1,2dihydro-1-arylnaphtho[1,2e][1,3]oxazine-3-one derivatives under thermal and solvent-free conditions using silica supported phosphotungustic acid.

EXPERIMENTAL

All reagents were purchased from Merck and commercial vendor and used without further purification. The reaction was monitored by TLC using 0.2 mm Merck silica gel 60 F254 precoated plates, which were visualized with UV light. Melting points were measured on an Lab-India MR.Vis⁺ apparatus. The 1H-NMR spectra were determined 300 MHz instrument.

GENERAL PROCEDURE

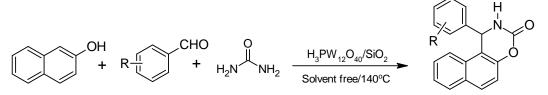
Preparation of Silica supported phosphotungustic acid

Silica preparation: The silica gel (80-200 mesh size) was washed with 1M HCl solution and followed washed with distilled water, 30% H₂O₂, and then again washed with distilled water. After all washing, the isolated silica was dried overnight at 373k under full vacuum to give preconditioned active silica gel for catalyst support.

Catalysts were prepared by the impregnation method. In a typical example, 1.2g of phosphotungustic acid, 2.0 g of the preconditioned silica gel, and 20 mL of distilled water were put into a 100mL round bottom flask, the resulting mixture was refluxed with magnetic stirring for 5 h at 100°C, then evaporated to dryness at 90°C, and followed by dry in an oven at 100°C for 5 h. The loading amount was exactly 60 wt%. The catalysts should be calcined for 1 h at $200^{\circ}C^{xxxi}$ before use.

General procedure for the preparation of 1,2-dihydro-1-arylnaphtho[1,2 e][1,3]oxazine-3-one derivatives (scheme-1)

A mixture of β -naphthol (0.01 mol), aldehyde (0.01 mol), urea (0.012 mol), H₃PW₁₂O₄₀/SiO₂ (10 mol %) and heated with stirring at 140°C in an oil bath. The reaction was monitored by TLC. After cooling, the reaction mixture was dissolved in ethyl acetate and the mixture stirred for 10 min. The suspended solution was filtered and the heterogeneous catalyst was recovered. The ethyl acetate was evaporated and the crude product crystallized in MeOH to afford the pure product.



R= H, CH3, OH, OMe, F, Cl, Br, NO2

Scheme-1: Green synthesis of naphthoxazinone on $H_3PW_{12}O_{40}$. Si O_2 under solvent free conditions.

Selected spectral data

1-(4-Methoxy-Phenyl)-1,2-dihydro-naphtho[1,2-][1,3]oxazin-3-one (*Table 1 entry; c*) MP = 187–188 °C; ¹H NMR (300 MHz, DMSO-d6): d= 3.73 (s, 3H), 6.13 (d, 1H), 6.87 (d, 2H), 7.12-7.25 (m, 3H), 7.38-7.45 (m, 2H), 7.64 (d, 1H), 7.73-7.77 (m, 1H), 8.05-8.13 (m, 1H), 8.53 (s, 1H).

1-(4-Fluro-Phenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (Table 1 entry; f) MP = 200-202°C; ¹H NMR (300 MHz, DMSO-d6): d = 6.21 (d, 1H), 6.97-7.10 (m, 2H), 7.14-7.24 (m, 3H), 7.33-7.42 (m, 2H), 7.63 (d, 1H, J=8.5Hz), 7.72-7.76 (m, 1H), 8.07-8.12 (m, 1H), 9.68 (s, 1H).

RESULT AND DISCUSSION

Characterization of the $H_3PW_{12}O_{40}/SiO_2$ catalysts : FT-IR spectra of the $H_3PW_{12}O_{40}/SiO_2$ series are shown in **Figure-1**. Pure $H_3PW_{12}O_{40}/SiO_2$ exhibited typically five major IR bands located at 1609, 1073, 972, 899 and 800-700 cm-1 for its Keggin structure. Supported catalyst was observed to feature the characteristic bands of Keggin structure. This result shows that the structure does not change after HPW supported on silica. Similar results were also observed by Newman et al^{xxxii}.

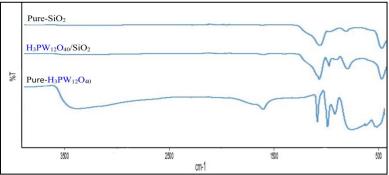


Figure-1: FT-IR spectra of H₃PW₁₂O₄₀, H₃PW₁₂O₄₀/SiO₂ and SiO₂

XRD patterns of the $H_3PW_{12}O_{40}/SiO_2$ series are shown in Figure-2. The diffraction peaks of Keggin structure in $H_3PW_{12}O_{40}$ appeared at 21-23°, 26-27°, 30-31° and 35-36°. No diffraction peaks detected on the pure SiO2 but when the $H_3PW_{12}O_{40}/SiO_2$ loading, diffraction peaks of catalysts appeared. This result indicates that the surface of silica is accumulated by crystallites of $H_3PW_{12}O_{40}$ gradually. All the three $H_3PW_{12}O_{40}$, SiO₂ and $H_3PW_{12}O_{40}/SiO_2$ XRD patterns are shown in figure-2.

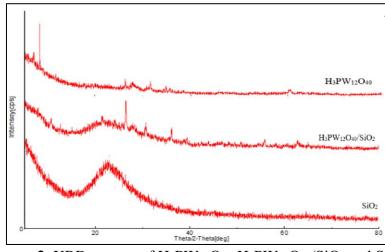
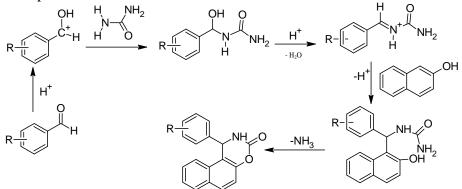


Figure-2: XRD spectra of H₃PW₁₂O₄₀, H₃PW₁₂O₄₀/SiO₂ and SiO₂

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Catalyst activity: In this article, we report a new, simple, mild and effective procedure for the one-pot synthesis of naphthoxazinone derivatives using $H_3PW_{12}O_{40}/SiO_2$ as a heterogeneous and recyclable catalyst. This catalyst is easy to handle, safe and environmentally favorable. The reaction was carried out between 2-naphthol, aromatic aldehydes and urea in the presence of mentioned catalyst (Scheme-1).

As a results of our experiments we found that aromatic aldehydes containing both electrondonating groups or electron-withdrawing groups (including halide groups) reacted well to give the corresponding 1,2-dihydro-1-arylnaphtho [1,2-e] [1,3]oxazine-3-ones in good yields. The results are summarized in Table-1 and the proposed reaction mechanism that accounts for the novel multi-component reaction is shown in scheme-2.



Scheme-2: Proposed mechanism for the synthesis of b-naphthalene condensed oxazinone derivatives.

In this reaction is the condensation of aldehyde and urea to give reactive acylimine intermediate. Subsequently, the resulting acylimine intermediate undergoes a cyclization with 2-naphthol affording the corresponding products and ammonia.

Table-1: Reaction of 2-naphthol with various aromatic aldehydes and urea.

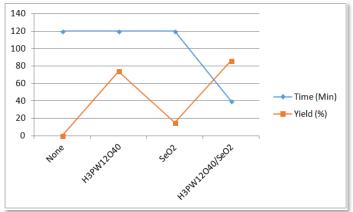
Sr.no	Aromatic Aldehyde	Product	Reaction time (min)	Yield (%) ^a	Observed Melting point (°C)	Reference Melting point (°C)
a	СНО	H-Z O	40	86	218-220	219-222 ^{xxvii}
b	но-{	HO, H, O	50	87	182-184	181- 182 ^{xxxiii}
с	МеО-СНО	MeO H N O	60	84	187-188	185-187 ^{xxx}
d	H₃C-√−СНО	H ₃ C H ₁ C H ₁ O H ₂ O	60	82	170-172	171-173 ^{xxvii}

e	СІ———СНО		40	92	212-214	213-215 ^{xxvii}
f	FСНО		45	87	200-202	197- 200 ^{xxxiv}
g	Br————————————————————————————————————	Br H-P O	50	90	218-221	221- 223 ^{xxxiii}
h	О ₂ N-СНО		40	80	228-230	226- 227 ^{xxxiii}

^a Yields refer to the pure isolated products.

In order to investigate the high catalytic activity of $H_3PW_{12}O_{40}/SiO_2$ in compared to $H_3PW_{12}O_{40}$, SiO2 and $H_3PW_{12}O_{40}/SiO_2$, we have performed a model study using benzaldehyde, 2-naphthol and urea by use of certain value of catalysts at 140°C under solvent-free conditions (figure-3).

Figure-3: Reaction of benzaldehyde, 2-naphthol, and urea in diverse catalytic conditions at $140^{\circ}C$



Reaction was carried out under solvent free condition. Yield claimed on isolation basis.

Figure-3 clearly illustrates that among four mentioned catalysts, silica supported phosphotungustic acid is an effective catalyst in terms of reaction times and yields of product, because of the supported SiO_2 increase contact surface of materials. To show the merit of the present work in comparison with the previously reported, we compared results

 $H_3PW_{12}O_{40}/SiO_2$ with other catalysts in the synthesis of 1,2-dihydro-1-arylnaphtho[1,2-e][1,3]oxazine-3-one. As shown in table-2, $H_3PW_{12}O_{40}/SiO_2$ can act as effective catalyst with respect to reaction times, yields and the obtained products.

While comparing the $H_3PW_{12}O_{40}/SiO_2$ with other existing reported catalyst (table-2), clearly illustration that among all catalysts $H_3PW_{12}O_{40}/SiO_2$ is effective catalyst in terms of isolated yield and reaction time.

Entry	catalyst	condition	Time (h)	Yield ^a (%)
1	ZnO NPs ²⁵	Solvent-free; 150 °C; catalyst (0.3 equiv)	1h	90
2	TMSCl ²⁴	DMF; 140 °C; catalyst (10 mg)	12h	83
3	HClO ₄ /SiO ₂ ²⁷	Solvent-free; 150 °C; catalyst (2 mol %)	1h	88
4	PTSA ³⁰	Solvent-free; 160 °C; catalyst (0.3 mmol)	1.5h	63
5	phosphomolybdic acid ²⁶	DMF; 100°C; catalyst (0.001 mmol)	3h	89
6	$H_3PW_{12}O_{40}/SiO_2{}^b$	Solvent-free; 140 °C; catalyst (10 mol %)	40min	92

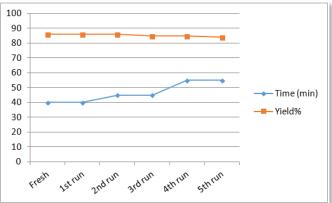
Table-2: Comparison of the results of using $H_3PW_{12}O_{40}$. SiO₂ with other catalyst.

^a Based on 4-Chlorobenzaldehyde (0.01 mol), 2-naphthol (0.01 mol) and urea (0.012 mol). ^b This work.

To determine the optimum quantity of $H_3PW_{12}O_{40}/SiO_2$ in reaction of 4-chloro benzaldehyde, 2-naphthol and urea under thermal and solvent free conditions, we used different amounts of catalyst including 5, 10, 15 and 20 mol% of silica supported phosphotungustic acid. It is observed that the excellent results were obtained 10 mol % $H_3PW_{12}O_{40}/SiO_2$ at 140 °C in 40min.

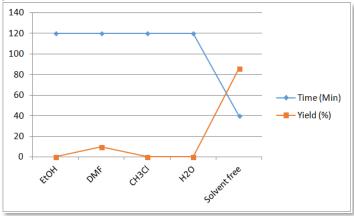
To evaluate the stability of the catalytic activity and the potential for recycling, we completed several catalytic cycles. In each cycle, $H_3PW_{12}O_{40}/SiO_2$ was washed with ethanol and dried under vacuum to remove the residual solvent. The catalyst could be reused for five times with a minimal loss of activity (Figure-3).

Figure-4: The catalyst reusability for the synthesis of naphthoxazinone from benzaldehyde, 2-naphthol, and urea.



In order to survey the effect of the solvents on the preparation of naphthoxazinone derivatives, the reaction of benzaldehyde, urea and 2-naphthol was carried out in various solvents (Figure -5). It is observed that the excellent results were obtained in solvent-free conditions at 140 °C using $H_3PW_{12}O_{40}/SiO_2$ as catalyst.

Figure-5: *Effect of solvents on the preparation of 1,2-dihydro-l-phenylnaphtho[1,2-e][1,3]-oxazine-3-one at reflux conditions.*



CONCLUSION

In conclusion, we demonstrated that silica supported phosphotungstic acid is a new, efficient and green catalyst for the synthesis of naphthoxazine-3-one derivatives. The one-pot threecomponent condensation of aromatic aldehydes, 2-naphthol and urea in the presence of $H_3PW_{12}O_{40}/SiO_2$ afforded naphthoxazinones under thermal solvent-free conditions. The distinguished features of this method are shorter reaction times, simple work-up, eco-friendly, excellent isolated yield, cost effective recovery and reusability of catalyst for a number of times without appreciable loss of activity in comparison with other reported methods.

We strongly hope that the highly stable $H_3PW_{12}O_{40}/SiO_2$ catalyst could give the way for the production of naphthoxazinones and its derivatives and create the platform for the commercialization of the process by replacing the existing homogenous catalysts which suffered from various drawbacks such as corrosion, hazardous to handle, waste production, huge effluent, environment hazard and high cost.

ACKNOWLEDGMENT

The author thanks the department of chemistry and colleague student, Dr. A.P.J. Abdul Kalam University, Indore. for their constant encouragement and support for this work.

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Received on october13, 2022.