Iranian Journal of Catalysis 6(2), 2016, 99-105

IRANIAN JOURNAL OF CATALYSIS

Environmentally benign synthesis of 1,8-dioxooctahydroxanthene derivatives using 10-molybdo-2-vanadophosphoric acid as an efficient and reusable catalyst under solvent-free condition

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Received 11 June 2015; received in revised form 26 September 2015; accepted 27 September 2015

ABSTRACT

A green and efficient protocol for the synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydroxanthene derivatives via cyclocondensation of 5,5-dimethyl-1,3-cyclohexanedione and aromatic aldehydes in the presence of catalytic amount of 10-molybdo-2-vanadophosphoric acid under solvent-free conditions has been described. The 10-molybdo-2-vanadophosphoric acid was prepared and characterized by FT-IR spectroscopy, thermal analysis and XRD analysis techniques. Characterization of the catalyst by FT-IR spectroscopy confirms the substitution of two Mo^{6+} ions by a V^{5+} ion in a Keggin structure. The effect of various reaction parameters on the rate of reaction was investigated. The reaction was carried out without using any solvent and the process subscribes to the principles of green chemistry. Moreover, the present protocol offers several advantages such as simple work-up, shorter reaction time, excellent yields, recovery and reusability of catalyst.

***Keywords**: 1,8-Dioxooctahydroxanthenes; Heteropoly acids; 10-Molybdo-2-vanadophosphoric acid; Heterogeneous catalyst; Solvent-free.*

1. Introduction

Heteropoly acids (HPAs) are a unique class of nanosized metal-oxygen cluster anions [1]. HPAs are widely used as homogeneous and heterogeneous acid and oxidation catalysts due to their high thermal stability, strong acidity and strong oxidizing ability [2]. They are highly soluble in polar solvents but insoluble in non-polar ones. Some advantages of HPAs are non-corrosive nature, multifuctionality, strong Bronsted acidity, structural mobility, reusability, non-toxicity and experimental simplicity [3]. Among the wide range of heteropoly compounds, the Keggin-type are most stable and more easily available [4]. The Keggin type HPAs are typically represented by the formula H_{8-x} $[XM_{12}O_{40}]$, where X is the hetero atom (usually P^{5+} or Si^{4+}), x is it's oxidation state and M is its addenda atom (most frequently W^{6+} or Mo^{6+}). The M^{6+}ions can be substituted by many other metal ions, e.g., V^{5+}, Co^{2+}, Zn^{2+} etc [5]. When, molybdenum atoms of 12-molybdophosphoric acid are partly substituted by vanadium atoms, the acid strength decreases along with its thermal stability [6]. The 10-molybdo-2-vanadophosphoric acid is quite intensively studied polyoxometalate of the Keggin structure, known for its strong Bronsted acidity and redox-type activity [7].

Xanthenes derivatives are parent compounds of a large number of naturally occurring and synthetic derivatives and occupy a prominent position in medicinal chemistry [8]. They are used as dyes [9], fluorescent materials for visualization of bio-molecules and laser technologies due to their useful spectroscopic properties [10]. The synthesis of xanthenes have also received significant attention of organic chemist essentially because of their wide ranging biological and therapeutic properties such as antibacterial [11], antiviral [12], anti-inflammatory activities [13] as well as efficiency in photodynamic therapy and antagonist for the paralyzing action of zoxazolamine [14]. Various reports are available in literature for the synthesis of 1,8-dioxooctahydroxanthene derivatives

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using 5,5-dimethyl-1,3-cyclohexadione, aromatic aldehydes and catalysts such as p-toluenesulphonic acid (p-TsOH) in organic solvents [15], amberlyst [16], $FeCl_3.6H_2O$ in ionic liquid [17], $InCl_3.4H_2O$ [18], $NaHSO_4.SiO_2$[19], PPA-SiO_2 [20], p-dodecylbenzene sulphonic acid (DBSA) in aqueous media [21], trimethylsilyl chloride [22] and triethylbenzyl ammonium chloride [23]. However, some of these methodologies are associated with several shortcomings such as application of expensive and toxic catalysts, long reaction times, harsh reaction conditions, low product yield, difficulty in recovery and reusability of the catalysts. Therefore, introducing clean processes and utilizing eco-friendly and green catalysts which can be simply recycled at the end of reactions is still important.

The present study deals with the preparation of 10-molybdo-2-vanadophosphoric acid and its characterization by FT-IR spectroscopy, thermal analysis and XRD analysis techniques. The synthesized catalyst was used for the synthesis of 3,3,6,6-tetramethyl- 9- aryl- 1,8- dioxooctahydroxanthene derivatives by the reaction of 5,5-dimethyl-1,3-cyclohexadione and aromatic aldehydes under solvent-free conditions (Scheme 1).

2. Experimental

2.1. Characterization techniques

FT-IR spectra were obtained with a Bruker, Germany (Model 3000 Hyperion microscope with vertex 80 FT-IR system) spectrometer. XRD patterns were obtained with a Philips X'pert MPD System instrument using Cu Kα radiation. The TG-DTA measurements of the samples were made with the Thermal Analyzer (Perkin Elmer, Model Diamond TG-DTA) with about 10 mg of sample in a platinum crucible at a heating rate of 10 °C min^{-1} in an air atmosphere. ^{1}HNMR spectra were recorded on a Bruker Avance 400 and ^{13}CNMR were recorded on a Bruker DRX-300 instrument using TMS as an internal reference. Mass spectra were recorded on Waters UPLC-TQD Mass spectrometer using electrospray ionization technique. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath.

2.2. Preparation of 10-molybdo-2-vanadophosphoric acid $H_5[PMo_{10}V_2O_{40}]$ $30H_2O$

Sodium metavanadate (24.4g, 0.20 mol) was dissolved by boiling water (100 ml) and then mixed with Na_2HPO_4 (7.1 g, 0.050 mol) in water (100 ml). After the solution was cooled, concentrated sulfuric acid (5 ml) was added, and the solution developed a red colour. An addition of $Na_2MoO_4.2H_2O$ (121 g, 0.50 mol) dissolved in water (200 ml) was then made. While the solution was vigorously stirred, concentrated sulfuric acid (85 ml) was added slowly, and the hot solution was allowed to cool at room temperature. The 10-molybdo-2-vanadophosphoric acid was then extracted with diethyl ether (500 ml). Air was passed through the heteropoly etherate to free of diethyl ether. The solid remaining was dissolved in water, concentrated to first crystal formation in a vacuum desiccator over concentrated sulfuric acid, and then allowed to crystallize further. The large red crystals that formed were filtered, washed with water and air dried (yield, 30% based on molybdate) [24].

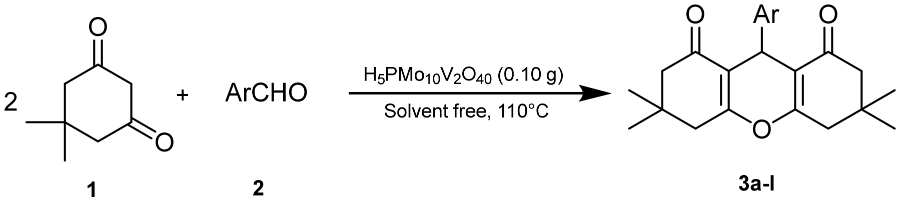
2.3. General procedure for the synthesis of 1,8-dioxooctahydroxanthene derivatives

The 5,5-dimethyl-1,3-cyclohexanedione (2 mmol), an aromatic aldehyde (1mmol) and $H_5PMo_{10}V_2O_{40}$ (0.1 g) was heated in the oil bath at 110°C for the appropriate time. The progress of reaction was monitored by thin layer chromatography (TLC). Upon completion, the reaction mixture was cooled to room temperature and ethanol (10 ml) was added. The catalyst was recovered from filtrate. The residue was washed with ethanol (95%) to give compounds 3a-l in high yields. Recovered catalyst was washed with diethyl ether (10 ml) and calcined at 120°C for 1h, before reusing.

3. Results and Discussion

3.1. Characterization of $H_5PMo_{10}V_2O_{40}$ catalyst

The primary structure of $H_5PMo_{10}V_2O_{40}$ was identified by four characteristic IR bands appearing in the range of 700-1200 cm^{-1} (Fig. 1). The four characteristic IR bands of $H_5PMo_{10}V_2O_{40}$ appeared at 1063 cm^{-1} (P-O stretching), 962 cm^{-1} (M=O stretching), 865 cm^{-1} (inter-octahedral M-O-M stretching) and 780 cm^{-1} (intra-octahedral M-O-M stretching) [25].



Scheme 1. Synthesis of 1,8-dioxooctahydroxanthene derivatives using $H_5[PMo_{10}V_2O_{40}]$ $30H_2O$.

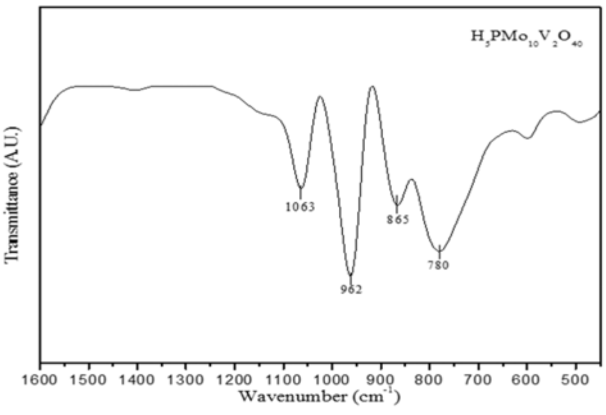


Fig. 1. FT-IR spectra of the $H_5PMo_{10}V_2O_{40}$ catalyst.

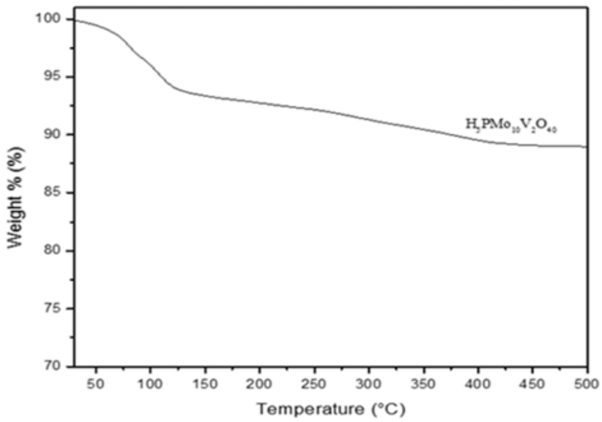


Fig. 2. Thermal analysis of $H_5PMo_{10}V_2O_{40}$ catalyst.

The thermal stability of $H_5PMo_{10}V_2O_{40}$ catalyst was examined by thermal analysis under air flow (Fig. 2). The TGA of $H_5PMo_{10}V_2O_{40}$ showed a mass loss of about 7% up to a temperature of 130°C, indicating loss of free and adsorbed water. The gradual mass loss of about 4% up to 500°C due to the release of more hydrated or structural water. Fig. 3 shows the XRD pattern of $H_5PMo_{10}V_2O_{40}$ catalyst.

The XRD pattern of $H_5PMo_{10}V_2O_{40}$ showed a highly intense peak 2θ = 8.90°, 27.98° corresponding to the basal d-spacing (d_{001}) of about 9.91 and 3.18 Å. Several other peaks are also observed which indicates that $H_5PMo_{10}V_2O_{40}$ was crystalline in nature.

3.2. Catalytic activity

To optimize the reaction conditions, the reaction of 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) and benzaldehyde (1 mmol) under solvent-free conditions was selected as a model. After many studies on the above model reaction, we found that when less than 0.1 g of $H_5PMo_{10}V_2O_{40}$ was applied, the corresponding products obtained in lower yields and require more time (Table. 1, entries 1-3), whereas use of more than 0.1 g catalyst did not improve the yield and require same time (Table. 1, entries 5-6). This was due to the fact that beyond a certain concentration, there exist an excess of catalyst sites over what is actually required by the reactant molecules and hence, the additional catalyst does not increase the rate of reaction. Therefore, in all further reactions 0.1 g of $H_5PMo_{10}V_2O_{40}$ catalyst was used.

The effect of different temperature on model reaction also studied in presence of 0.1 g of $H_5PMo_{10}V_2O_{40}$ under solvent-free conditions. As can be seen from the results (Table. 2, entries 1-6), the yield of product was enhanced by increasing the temperature up to 110°C but thereafter, it was not enhanced on further increasing the temperature above 110°C.

The best result was obtained by carrying out the reaction of 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) and benzaldehyde (1 mmol) in presence of $H_5PMo_{10}V_2O_{40}$ (0.1 g) at 110°C under solvent-free condition.

In order to evaluate the generality of the process, we next carried out a series of reactions using 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) and various aromatic aldehydes (1 mmol) in presence of $H_5PMo_{10}V_2O_{40}$ (0.1 g) at 110°C under solvent-free conditions. Most importantly, aromatic aldehydes with substituent's bearing either electron-donating or electron-withdrawing groups as well as heterocyclic aldehydes reacted successfully in the presence of $H_5PMo_{10}V_2O_{40}$ as a catalyst. In all these reactions expected products were obtained in good to excellent yields. The results are shown in Table 3.

The suggested mechanism for the 10-molybdo-2-vanadophosphoric acid catalyzed synthesis of 1,8-dioxooctahydroxanthene is shown in Scheme 2. Concerning the reaction mechanism, we suggest that, initially activation of the carbonyl group of aldehyde by $H_5PMo_{10}V_2O_{40}$ catalyst facilitates nucleophilic attack of dimedone in its enol form and form corresponding carbocation. This carbocation was then reacts with the second activated dimedone to give intermediate, which then undergo dehydration to give the final product.

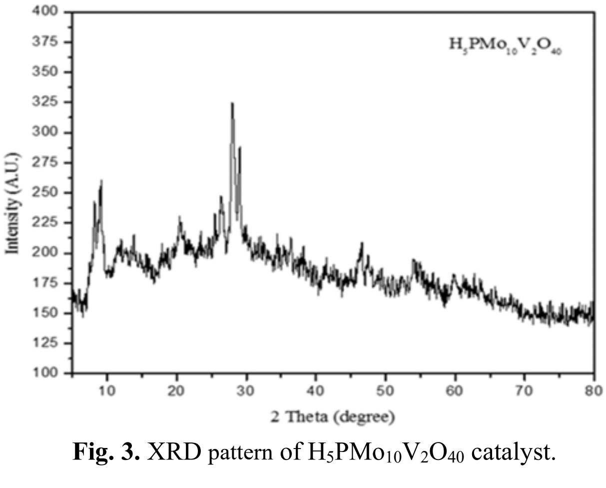


Fig. 3. XRD pattern of $H_5PMo_{10}V_2O_{40}$ catalyst.

Table 1. Effect of catalyst concentration on the synthesis of 1,8-dioxooctahydroxanthene.

Entry	Amount of catalyst (g)	Time (min)	Yield (%)[a]
1	0.025	65	50
2	0.050	45	78
3	0.075	25	85
4	0.100	15	93
5	0.125	15	93
6	0.150	15	93

Reaction conditions: 5,5-dimethyl-1,3-cyclohexanedione(2mmol), benzaldehyde (1 mmol) and H5PMo10V2O40 under solvent-free conditions.

[a]Isolated yield.

To show the merit of the present work, we compared our results with Mg-Al hydrotalcite [31], ionic liquid [bmim] ClO4 [32], β-cyclodextrin [33], alum [30], trichloroisocyanuric acid [10] and diammonium hydrogen phosphate [34] in the synthesis of 3,3,6,6-tetramethyl- 9-aryl- 1,8- dioxooctahydro xanthene derivatives. The Table 4 clearly demonstrates that $H_5PMo_{10}V_2O_{40}$ is an effective catalyst in terms of reaction time and yield of obtained product relative to other reported catalysts. Thus, the present protocol with $H_5PMo_{10}V_2O_{40}$ catalyst is convincingly superior to the previous reported catalytic methods.

3.3. Recyclability of the catalyst

In order to check the recyclability of catalyst after the completion of reaction, the reaction mixture was cooled to room temperature and hot ethanol was added. The catalyst was recovered from filtrate. Recovered catalyst was washed with diethyl ether (10 ml) and calcined at 120°C for 1h, before reusing. We found that the catalyst could be reused at least three times for the synthesis of 3a and afforded comparable yields of 91, 88 and 84% confirming the recyclability and reusability of the catalyst in this reaction. The protocol described herein is advantageous in terms of preclusion of hazardous organic solvents, catalytic amount of reagents, shorter reaction time, good yields, recovery and reusability of catalyst.

4. Conclusion

We have demonstrated that 10-molybdo-2-vanadophosphoric acid is an efficient and reusable catalyst for the synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydroxanthene derivatives. The salient features of this protocol include the use of a catalytic amount of the 10-molybdo-2-vanadophosphoric acid, good yields, operational simplicity, short reaction times, catalyst separation from the reaction medium and catalyst reusability. Moreover, the use of environmentally benign catalyst and avoidance of hazardous organic solvents are important features of this method.

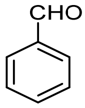
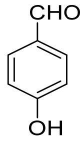
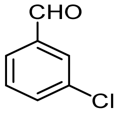
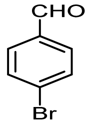
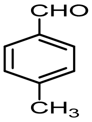
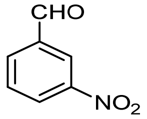
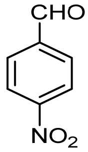
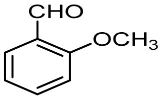
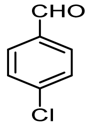
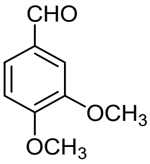
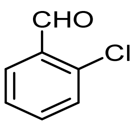
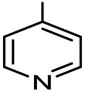
Table 2. Effect of temperature on the synthesis of 1,8-dioxooctahydroxanthene.

Entry	Temp. (°C)	Time (min)	Yield (%)[a]
1	25	120	trace
2	50	90	48
3	80	50	74
4	100	25	86
5	110	15	93
6	120	15	93

Reaction conditions: 5,5-dimethyl-1,3-cyclohexanedione(2mmol), benzaldehyde (1 mmol) and $H_5PMo_{10}V_2O_{40}$ (0.1 g) under solvent-free conditions.

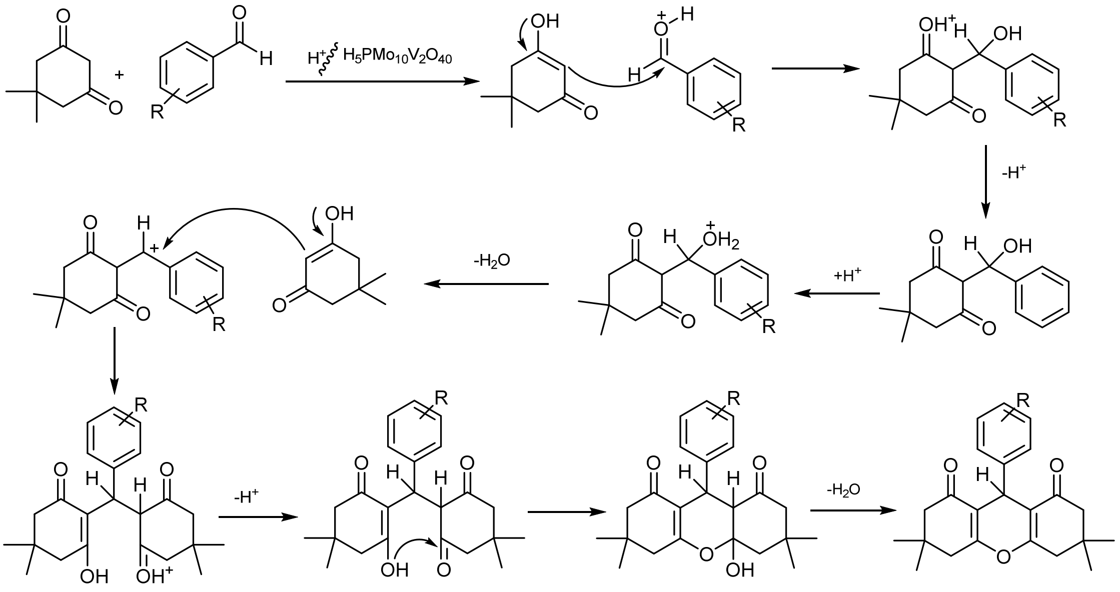
[a]Isolated yield.

Table 3. Synthesis of 1,8-dioxooctahydroxanthene derivatives using $H_5[PMo_{10}V_2O_{40}]$ $30H_2O$ as a catalyst.

Entry	Aldehyde	Product	Time (min)	Yield (%)[a]	m.p. (°C)		Ref.
					Found	Reported	
1		3a	15	93	203-204	204-205	[26]
2		3b	24	95	247-248	246-248	[27]
3		3c	20	89	180-182	182-184	[26]
4		3d	22	94	233-235	234-236	[27]
5		3e	18	95	214-216	217-218	[27]
6		3f	23	96	169-171	170-173	[26]
7		3g	20	92	223-225	223-224	[28]
8		3h	12	91	187-189	190-191	[29]
9		3i	14	94	225-227	226-228	[30]
10		3j	17	92	182-183	184-185	[28]
11		3k	21	91	224-226	226-228	[30]
12		3l	16	89	214-215	218-220	[27]

Reaction conditions: 5,5-dimethyl-1,3-cyclohexanedione (2 mmol), aromatic aldehyde (1 mmol) and $H_5PMo_{10}V_2O_{40}$ (0.1 g) at 110 °C under solvent-free conditions.

[a] Isolated yield.



Scheme 2. Proposed mechanism for the $H_5[PMo_{10}V_2O_{40}]$ $30H_2O$ catalyzed synthesis of 1,8-dioxooctahydroxanthenes.

Acknowledgments

One of the authors (T. K. Chondhekar) is thankful to UGC, New Delhi, India for awarding UGC-BSR faculty fellowship. We are thankful to the Head, Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad and Principal, Jawaharlal Nehru Engineering College, Aurangabad-431 004 (MS), India for providing the laboratory facility.

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