

Phosphomolybdic Acid: An Efficient and Easy Catalyst for Condensation of Thiazolidine-2, 4-Dione with Aldehydes under Mild Conditions

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Abstract: The condensation reaction of thiazolidine-2, 4-dione with aromatic aldehydes were carried out with phosphomolybdic acid in water, at room temperature in shorter times with higher yields is described. Herein, we have used water as a solvent which is a green solvent.

Keywords: Thiazolidine -2, 4 -dione; phosphomolybdic acid; condensation; green chemistry.

1 Introduction

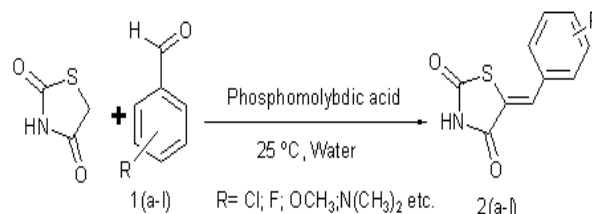
Literature reported that the Knoevangel condensation is one of the very important reaction used for the synthesis of various biologically potent compounds. It is mainly used for the formation of C=C bond [1]. This reaction is between active methylene compounds and carbonyl compounds for the synthesis of several therapeutic drugs, such as nifedipine and nitrendipine [2]. This reaction is performed using bases, such as amines, ammonia, or sodium ethoxide in various organic solvents like acetonitrile [3-5]. Lewis acids [6], zeolites [7] and heterogeneous catalysts [8-13] can also be used perform the reactions as per the literature. However, the reported procedures have some demerits; like, their less efficiency, can't be reused. Therefore, manipulation in methodologies has to be done to perform the Knoevangel condensation better in organic [14, 15].

Heteropoly acids (HPAs) are potential reagents due to their enough acidic character as well their oxidizing nature. Further, they also very popular catalyst due to their oxidizing capability in various organic transformation [16-19]. Catalysis using HPAs has to be explored in the research area of catalysis [20-23]. Literature reported that HPAs are known as environmentally benign solid catalyst as they are proven to show high catalytic ability, acidic character and selectivity to various reactions. Advantages of using HPAs under homogenous condition lies in their high solubility in polar solvent such as water, ethylacetate, ethanol, etc. HPAs can be recycled after the use in reaction [24]. In last two decades, a lot efforts has been done by researchers, academicians to explore the use of HPAs in

synthetic organic chemistry [25-28].

There is urgency to develop simple and effective methodology for the synthesis of thiazolidine-2, 4-dione derivatives that come under the "Green Chemistry". Further, it is very important to use the green solvents like water and it is the most economical and eco-friendly solvent to carry out the organic reactions.

Although, due to low solubility of reactants in water as well unsuitability of certain intermediate or race between the desired reaction and hydrolysis restrict the use of water as a common solvent. Still many reactions have been performed and reported using water as a solvent [29, 30]. Herein, we have reported a methodology for the condensation reaction between thiazolidine-2, 4-dione and aldehydes in water using phosphomolybdic acid as a catalyst (Scheme 1)



Scheme 1 Reaction between of thiazolidine-2, 4-diones and aromatic aldehyde

2 Results and Discussion

2.1 Catalyst characterization

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2.1.1 Thermal analysis

The catalyst was initially characterized by thermal analysis methods as in **Fig. 1**. The degree of hydration of the catalyst (phosphomolybdic acid), was determined from TGA analysis and corresponded to the formula ($H_5PMo_{12}O_{40}.xH_2O$). The TGA of the phosphomolybdic acid (Fig. 1) shows first decomposition at 69.7°C indicating loss of six molecule of water, which is water of crystallization (11.34 % weight loss experimentally and 11.74 % weight loss theoretically).

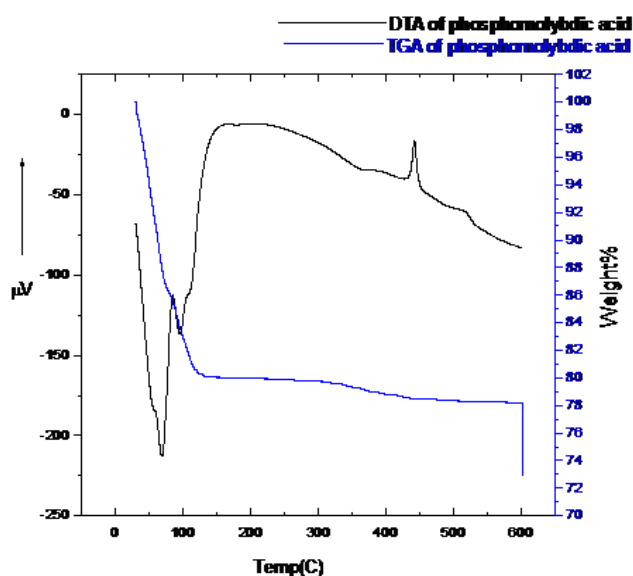


Figure 1 TG/DTA of Phosphomolybdic acid.

At 91.86°C there is a loss of two molecules of water that indicates 4.2% weight loss theoretically and 4.46 % loss experimentally. Moreover, at 440.31°C there was a loss of another two water molecules, which indicates 4.45 % weight loss experimentally and 5.26 % weight loss theoretically and we finally get mixture of oxide of P and Mo at 590°C with a loss of another two water molecules. From the percentage weight loss the number of water molecules were calculated to be ten H_2O molecules.

It has been already been reported that the degree of hydration in heteropoly compounds depends on various factors such as relative humidity, solution acidity, degree of drying, temperature etc. From DTA curve, we observed endothermic peak at 69.77°C and 91.86°C while at 440.31°C an exothermic peak was observed.

2.1.2 Infrared spectra

The infrared spectra of phosphomolybdic acid exhibit bands in the range of 3392 cm^{-1} due to ν (O-H) for water of crystallization and constitutional water present in phosphomolybdic acid (Fig. 2). Apart from these bands phosphomolybdic acid shows major peaks at 961 cm^{-1} and 782 cm^{-1} , due to P-O-Mo and P-O-P respectively as in **Fig. 2**.

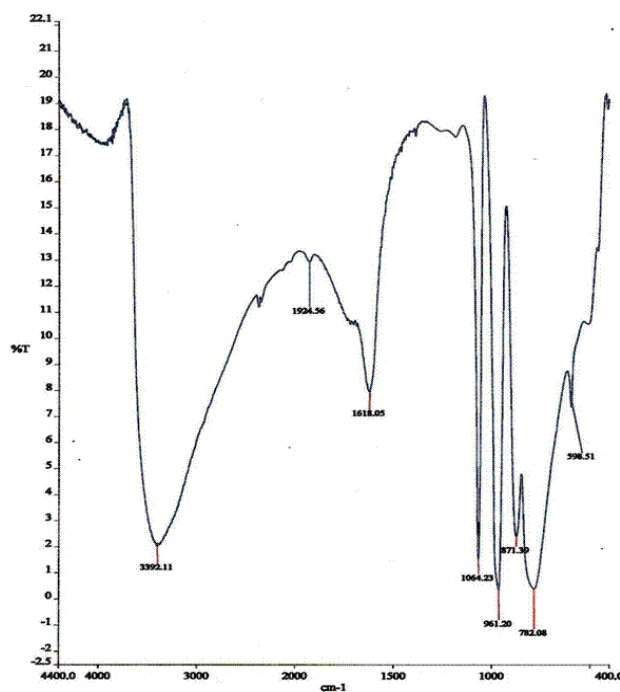


Figure 2 IR of phosphomolybdic acid

2.1.3 X-ray diffraction

The X-ray diffraction pattern of phosphotungstic acid is shown in **Fig. 3**. X-ray powder analysis is used widely to study the structure of phosphomolybdic acid. The X-Ray diffraction curve was taken in the 2θ ranges of 5° to 70° . The 2θ values are 26.545° , 33.310° , 44.685° and 44.825° with relative intensity counts in percentage of 65.2, 25.5, 100.0 and 44.2 respectively. So according to the curve, the high intensity counts of the peak pattern of the XRD confirm the crystalline nature of the phosphomolybdic acid.

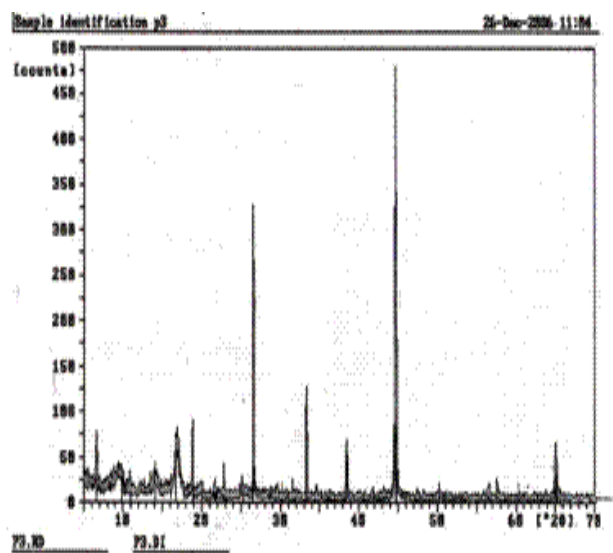


Figure 3 XRD of Phosphomolybdic acid

2.2 Optimization of catalyst

In order to find out the best catalyst for the reaction between thiazolidine-2, 4-dione and benzaldehyde, we carried out the reaction with different catalyst in water as a solvent. We observed that phosphomolybdic acid as a best catalyst for the reaction between thiazolidine-2, 4-dione and benzaldehyde in water as a solvent as in **Table 1**.

Table 1 Optimization of the catalyst for the reaction between of thiazolidine-2, 4-diones and benzaldehyde ^a

Entry	Catalyst	Time (min)	Yield (%)
1	-	45	35
2	Phosphomolybdic acid	20	93
3.	Boric acid	25	70
4	Indium chloride	35	82
5	Triflic acid	25	60

^a Reaction condition: thiazolidine-2, 4-dione (10 mmol), benzaldehyde (10 mmol), phosphomolybdic acid (10 mmol %), r. t., solvent (10 ml), stirred for 20 minutes.

2.3 Solvent effect

Table 2 Effect of solvent for the reaction between of thiazolidine-2, 4-diones and benzaldehyde ^a

Catalyst (mmol %)	Time (minutes)	Yield (%) ^b
2	20	58
5	20	71
10	20	92
15	20	85
20	20	72

^a Reaction condition: Thiazolidine-2, 4-dione (10 mmol), benzaldehyde (10 mmol), phosphomolybdic acid (10 mmol %), r. t., solvent (10 ml), stirred for 20 minutes; ^b Determined by GC.

In order to elucidate the role of the solvents, various solvents were used in order to evaluate the scope and limitations of the reaction. After screening different solvents, it was found that the best solvent in terms of fast conversion and quantified yield is water as in **Table 2** in all the phosphomolybdic acid catalyzed reaction for synthesis of thiazolidine-2, 4-dione derivatives.

2.4 Catalyst concentration

We observed that catalyst concentration also plays a detrimental role in catalyzing the coupling reaction for the synthesis of thiazolidine-2, 4-dione derivatives. By taking coupling of thiazolidine-2, 4-dione with benzaldehyde as model reaction and varying the concentration of phosphomolybdic acid in water and it was found that the optimum reaction rate and yield could be achieved at the catalyst concentration of 10 mmol% as in **Table 3**.

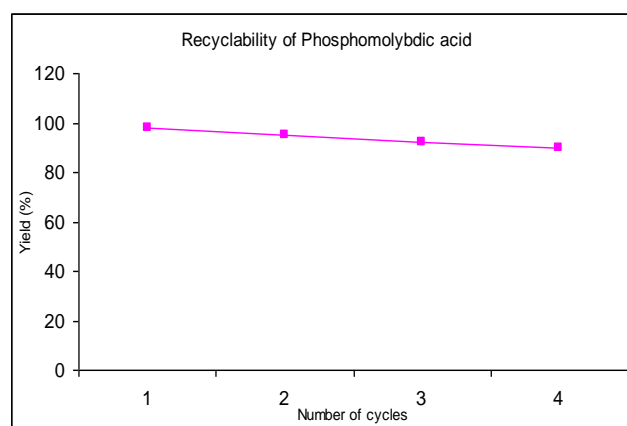
Table 3 Optimization of the amount of phosphomolybdic acid for the reaction between thiazolidine-2, 4-dione derivatives and benzaldehyde (**Table 4, Entry 1**) ^a

Solvent	Entry 1, Table 4	
	Time (minutes)	Yield (%) ^b
THF	20	80
DMF	20	70
DMSO	20	72
Methanol	20	91
Water	20	90

^a Reaction condition: Thiazolidine-2, 4-dione (10 mmol), benzaldehyde (10 mmol), phosphomolybdic acid (X mmol %), r. t., water (10 ml), stirred for 20 minutes; ^b Determined by GC.

2.5 Recycling of catalyst

A control experiment for the coupling of thiazolidine-2, 4-dione and benzaldehyde were conducted for showing recyclability of catalyst for four cycles. Herein the catalyst was recycled four times with the gradual decrease in activity as shown in **Graph 1**. The graph showed a little loss in activity of catalyst used in experiment. After completion of the reaction, the reaction mixture was centrifuged to pellet out the phosphomolybdic acid and it was washed with ethanol to remove all the organic impurities. The catalyst was reused for evaluating the performance in the next cycle. Only mild decreases in reaction yields in second cycle were observed. But there was gradual decrease in yield of product after fourth cycle. One explanation would be that the active catalyst is efficiently recycled but is of limited stability, resulting in progressively slower rates. Another would be that catalyst recycling is not as efficient as anticipated because of gradual oxidation of the phosphomolybdic acid. The same procedure was followed for different aldehydes for the synthesis of corresponding aldehydes as in **Table 4**.



Graph 1 Recycling of catalyst

Table 4 Reaction between thiazolidine-2, 4-dione and aldehydes using phosphomolybdic acid.

Entry	Reactant	Ar	Product	Conversion (%)	Yield (%)
1	1a	C ₆ H ₅	2a	98	90
2	1b	4-OCH ₃ C ₆ H ₄	2b	95	88
3	1c	4-OHC ₆ H ₄	2c	97	87

4	1d	2-OHC ₆ H ₄	2d	90	85
5	1e	2, 4- Cl ₂ C ₆ H ₃	2e	97	93

^a Reaction condition: Thiazolidine-2, 4-dione (10 mmol), aromatic aldehyde (10 mmol), phosphomolybdic acid (10 mmol %), r. t., water (10 ml), stirred for 20 minutes.

3 Experimental Section

3.1 Reagents and analysis

All reactions were carried out at ambient temperature in oven-dried glassware. The materials were purchased from Sigma-Aldrich and Merck and were used without any additional purification. All reactions were monitored by thin layer chromatography (TLC) on gel F254 plates. The silica gel (250-400 meshes) for column chromatography was purchased from Spectrochem Pvt. Ltd., India. ¹H-NMR and ¹³C-NMR (300 MHz) spectra were recorded in d₆-DMSO on a Bruker toxispin 300 MHz spectrometer (with TMS as internal references). Mass spectra were recorded on TOF-Mass spectrometer Model No. KC455.

The catalyst phosphomolybdic acid was systematically characterized by using analytical and spectroscopic technique such as thermo gravimetric analysis (TG-DTA on a DTA-60 Shimadzu) TG/DTA system under static air at a heating rate of 5°C min⁻¹ in N₂ atmosphere and The X ray diffraction patterns were recorded using a RIGAKU ROTAFLEX RAD-B by Rigaku corporation Japan diffractometer using Cu target CuK (α) 1 radiation with tube voltage 40kV and 60mA in 2θ ranging from 5° to 70°.

3.2 General procedure for the condensation between thiazolidine-2, 4-dione and benzaldehyde.

In a round bottom flask (50 ml), benzaldehyde (10 mmol) and thiazolidine-2, 4-dione (10 mmol) were taken and then 10 ml of water was added to the flask. Then phosphomolybdic acid (10 mmol %) was added to the above reaction mixture. The reaction was stirred at room temperature for a particular time till the solidification comes. Completion of the reaction was checked by the TLC. Then filter the reaction mixture and recrystallised it with methanol (Product: 2e; yield: 93 %). The filtrate was centrifuged at 3000 rpm for 10 minutes, so the phosphomolybdic acid was pelleted out and washed the catalyst with dilute ethanol to remove the organic impurity and the recovered catalyst was reused for evaluating the performance in the next cycle

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