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A green method for the synthesis of 2-aryl-1,3-dioxalanes/dioxanes and linear acetals using silica supported magnesium hydrogen phosphate ($MgHPO_4/SiO_2$)

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ABSTRACT

Silica supported magnesium hydrogen phosphate ($MgHPO_4/SiO_2$) has been used as a recyclable catalyst for the synthesis of some linear and cyclic aromatic acetals under solvent-free conditions. This novel method has advantages, such as high yield of products, simple work-up procedure and avoidance of the organic solvents, which will contribute it serving as a green process greatly.

Keywords: $MgHPO_4/SiO_2$, catalyst, solvent-free, acetals, aldehyde

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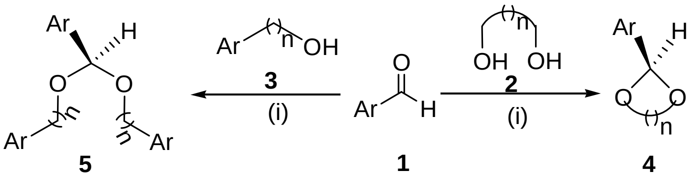
INTRODUCTION

Recently, solvent-free reactions are considered “green” because they eliminate a huge amount of waste (the spent solvent) and require less energy to isolate the product (solvent removal is obviously not an issue). Silica supported catalysts have also attracted the special attention of chemists [1-3] due to their eco-friendly nature, simple handling, recyclability, and high reactivity [4-6]. Similarly, protection of carbonyl functionaries from nucleophilic attack is one of the major problems faced during multistep syntheses. These problems remain a crucial challenge to organic chemists. A suitable method for solving this problem is the acetalization of carbonyl functions since acetals and 1,3-dioxanes are stable under neutral and basic conditions [7,8]. Besides the interest in acetals as protecting groups, many of them can serve for fragrances in cosmetics, pharmeceuticals, detergents, lacauer industries, and applications as food and beverage additives [9-11]. Until now several methods for the acetalization of the carbonyl function have been reported using ionic liquids [12-15], protonic acids such as HCl and H_2SO_4 and Lewis acids [16-19], and transitional metal complexes including Rh, Pd, and Pt [20,21]. Some of these strategies suffer from the drawback of green chemistry, and have been associated with several shortcomings such as use of corrosive protic acids and unrecyclable catalyst, long reaction times and low product yields, difficult work-up procedure, and the use of organic solvents. Therefore, presentation of a new, inexpensive and eco-friendly method for the protection of carbonyl functionality is an important topic, and one which is an active ongoing research area. There is a scope for the further improvement towards green reaction conditions and improved yields. We wish to report here a green and simple method for the protection of aromatic aldehydes **1** by diols **2** or aromatic alcohols **3** as 1,3-dioxanes, 1,3-dioxalanes **4**, and linear acetals **5** using a catalytic quantity of silica supported magnesium hydrogen phosphate under solvent-free conditions in excellent yields (Scheme-1).



(i): $MgHPO_4/SiO_2$, Grinding, rt
n: 1-3

Scheme-1

MATERIALS AND METHODS

General:

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. Yields refer to isolated pure products. The products were characterized by comparison of their spectral (IR and ^{1}H-NMR) and physical data with authentic samples which were produced by other reported procedures.

Preparation of silica supported magnesium hydrogen phosphate ($MgHPO_4/SiO_2$):

A 50 ml suction flask was equipped with a constant- pressure dropping funnel the gas outlet was connected to a vacuum system through an adsorbing solution (water) and an alkali trap. Anhydrous magnesium chloride (4.0 g, 40 mmol) was charged in the flask and concentrated phuosphoric acid (85%, 7.35 g, 40 mmol) was added dropwise over a period of 30 min at room temperature. HCI evolved immediately. After completion of the addition, the mixture was shaken for 30 min, while the residual HCI was eliminated by suction. The $MgHPO_4$ (5.48g) was obtained as white gel. The obtained solid acid was mixed by silica gel (6.43g).

General procedure for the synthesis of 4 and 5:

A mixture of 1 mmol of aldehyde, 1.5 mmol of diol or 2 mmol of aromatic alcohol, and $MgHPO_4/SiO_2$ (0.2 g) was added to a mortar. The mixture was thoroughly ground with a pestle at room temperature. The progress of the reaction was monitored by TLC (EtOAc/hexane, 1:3). After completion of the reaction, the mixture was dissolved in $CHCl_3$ (2 × 10 mL) and the catalyst was filtered. After evaporation of the solvent under reduced pressure and addition of ethanol and water, almost pure **4** and **5** were obtained in 90-98%. Further purification was achieved by recrystallization from the appropriate solvent. The catalyst was washed with diethyl ether, dried at 70 C for 45 min and reused in another reaction.

RESULTS AND DISCUSSION

A solvent-free reaction reduces pollution and cost due to simplification of experimental procedure, work up technique, and saving of labour. To exploit simple and suitable conditions for the synthesis of **4** and **5** using $MgHPO_4/SiO_2$ as an efficient solid acid catalyst, the treatment of benzaldehyde and ethanediol was chosen as a model reaction. Firstly, we found that in the absence of catalyst, the reaction did not proceed even at a high temperature (25-90 °C). After examining the various amounts of $MgHPO_4/SiO_2$, we found that the condensation reaction can be efficiently carried out by adding 0.2 g of the catalyst under grinding conditions at room temperature in a short time span of 10 min. The use of excessive amounts of the catalyst does not increase the yield or reaction rate (Table-1).

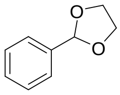
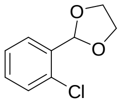
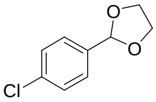
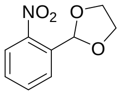
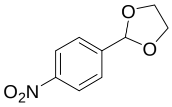
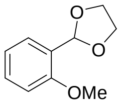
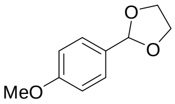
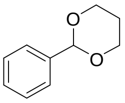
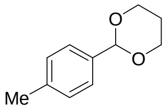
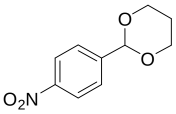
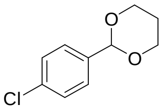
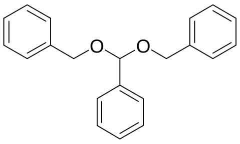
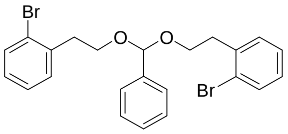
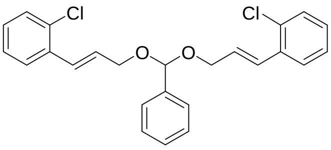
After optimization, the scope of this reaction was examined using a variety of aromatic aldehydes and aromatic alcohols and diols. It was found that both electron rich and electron poor aldehydes reacted well in this process to afford the corresponding products **4** and **5** in excellent yields. The obtained results are summarized in Table-2.

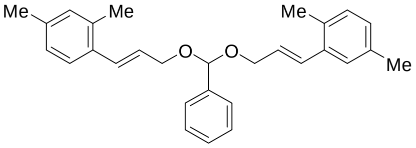
Table-1: Optimization of the amounts of $MgHPO_4/SiO_2$ under solvent-free conditions for the reaction of benzaldehyde with ethandiol

Entry	Catalyst amount (g)	Time (min)	Yield (%)[a]	Temp. (°C)
1	0.03	120	60	rt
2	0.05	120	75	rt
3	0.1	25	80	rt
4	0.2	5	98	rt
5	0.5	15	95	rt

[a] *Isolated yields.*

Table-2: Synthesis of 4 and 5 using $MgHPO_4/SiO_2$ under solvent-free conditions

Entry	Product	Time (min)	Yield (%)[a]	[Ref.]
4a		10	95	14
4b		10	90	13
4c		10	92	22
4d		18	95	22
4e		15	90	13
4f		12	88	22
4g		10	90	13
4h		12	90	14
4i		8	95	23
4j		16	90	23
4k		15	90	14
5a		5	95	19
5b		5	92	23
5c		10	95	23

5d		7	97	23

[a]*Isolated yields*

The main advantages of the presented protocol over existing methods can be seen by comparing our results with those of some previous reported procedures, as shown in Table-3.

Table-3: Comparison of our method with previous reported method in the synthesis of 4a

Entry	Conditions (Catalyst/Temperature (°C)/Solvent)	Time (min)	Yield (%)[a]	[Ref.]
1	Ionic liquid [SOClMIm]Cl/40/-	1200	80	15
2	In(OTf)3/ 80 (reflux)/ Benzene	180	92	18
3	Multi-SO_3H functionalized ionic liquids/25/-	180	96.5	13
4	SG-[$(CH_2)_3SO_3H$-HIM]HSO_4	90	95	12
5	Ionic liquid [TMPSA]HSO_4/ 25/-	30	77	14
6	SiO_2-SO_3H/68 (reflux)/*n*-hexane	60	58	24
7	$MgHPO_4/SiO_2$	10	95	This work

As can be concluded from Table 3, the present method is more appropriate than the others due to its excellent product yield in shorter reaction time without using organic solvents. In many cases, in order to achieve fast synthesis in an organic process, a catalyst must be used. The need to implement green chemistry principles (*e.g.* safer solvents, less hazardous chemical synthesis, atom economy, and catalysis) is a driving force towards the development of safe and reusable catalysts and avoidance of the use of organic solvents [25-28]. In this protocol, $MgHPO_4/SiO_2$ acts as a safe, highly efficient and recyclable catalyst under solvent-free conditions. It should be also mentioned that our efforts on the acetalization of aliphatic aldehydes and ketalization of aromatic ketones using silica supported magnesium hydrogen phosphate under similar conditions were unsuccessful. The problem with alkyl aldehydes is likely to be a result of their being enolisable.

CONCLUSION

To conclude, we present a new and green method for the synthesis of 1,3-dioxanes, 1,3-dioxalanes, and linear acetals by employing silica supported magnesium hydrogen phosphate as a safe, inexpensive and reusable solid acid catalyst under solvent-free conditions. Higher yields and shorter reaction times than the classical methods, and simple workup procedure are the appealing attributes of this work.

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