

## Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: <http://www.tandfonline.com/loi/lcyc20>

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To cite this article: Bandita Datta & M. A. Pasha (2011) Chemoselective Protection and Deprotection of Aldehydes Using Solid Supported Reagent (Silica Chloride) Under Solvent-Free Conditions, *Synthetic Communications*, 41:8, 1160-1166, DOI: [10.1080/00397911003797866](https://doi.org/10.1080/00397911003797866)

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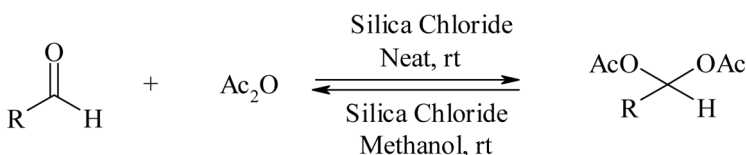
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## CHEMOSELECTIVE PROTECTION AND DEPROTECTION OF ALDEHYDES USING SOLID SUPPORTED REAGENT (SILICA CHLORIDE) UNDER SOLVENT-FREE CONDITIONS

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### GRAPHICAL ABSTRACT



**Abstract** Silica chloride, a heterogeneous catalyst, has been found to be an efficient catalyst for the protection of aldehydes as acylals under solvent-free conditions, and deprotection of acylals to aldehydes in methanol as a solvent occurred. The reaction takes a shorter time and ensures good to excellent yield of the products.

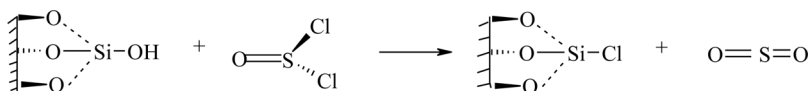
**Keywords** Acylals; aldehydes; deprotection in methanol; heterogeneous catalysis; silica chloride

## INTRODUCTION

Solid-phase synthesis<sup>[1]</sup> has become one of the most important tools in organic synthesis. The solid-phase chemistry concept has recently been used in a much wider sense to cover both solid-phase substrate and solid-phase reagent chemistry. Substrates are chemically bound to the surface of the solid support and then converted into the product, followed by liberation from the solid under the first approach.<sup>[2]</sup> In the second approach, the reagent is bound to the solid support; the solid-phase reagents can be either functionalized organic polymers<sup>[3]</sup> or silica-gel-grafted catalysts.<sup>[4]</sup> Compared to organic polymers, silica gel is strong enough to withstand harsh conditions.<sup>[5]</sup> The wide application of solid-supported reagents and catalysts is due to ease and safety in handling, rate enhancement, good yields, easy workup procedures, and economy. An inexpensive silica chloride can be prepared easily by treating thionyl chloride with silica gel<sup>[6]</sup> and is a better reagent when compared to thionyl

Received December 29, 2009.

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**Scheme 1.** Synthesis of silica chloride.

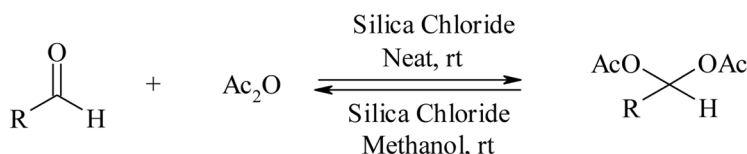
chloride or trimethyl silyl chloride (Scheme 1). Once the reaction gets completed, the catalyst can be filtered, washed with chloroform, and reused without decrease in activity for three runs.

In the preparation of many delicate organic compounds, some specific parts of the molecules cannot survive the required reagents or chemical environments; hence, these parts or groups must be protected.<sup>[7]</sup> The common carbonyl protecting groups are acetals,<sup>[8]</sup> ketals,<sup>[8]</sup> acylals,<sup>[9]</sup> and dithianes.<sup>[10]</sup> Acetals and ketals need acids, dithianes need metal salts or oxidizing agents for deprotection, whereas acylals need mild acid catalysts for deprotection.<sup>[11]</sup> Acylals are very robust to aqueous acid, neutral, and basic media.<sup>[12]</sup>

Acylals are used as building blocks in the synthesis of dienes required for Diels–Alder cycloaddition reactions,<sup>[13]</sup> and acylals have been applied as cross-linking reagents for cellulose in cotton and serve as activators in the composition of the bleaching mixture used for the treatment of wire-strained fibers<sup>[14]</sup> and as substrates in many organic reactions.<sup>[15]</sup>

A wide range of catalysts have been used to convert aldehydes into acylals; some of them are LiOTf,<sup>[16]</sup> Ceric ammonium nitrate (CAN),<sup>17</sup> InCl<sub>3</sub>,<sup>[18]</sup> H<sub>2</sub>NSO<sub>3</sub>H,<sup>[19]</sup> LiBF<sub>4</sub>,<sup>[20]</sup> H<sub>2</sub>SO<sub>4</sub>,<sup>[21]</sup> N-bromosuccinimide NBS,<sup>[22]</sup> SbCl<sub>3</sub>,<sup>[23]</sup> TMSCl–NaI,<sup>[24]</sup> FeCl<sub>3</sub>,<sup>[25]</sup> sulfated zirconia,<sup>[26]</sup> silica sulfuric acid,<sup>[27]</sup> Bi(NO<sub>3</sub>)<sub>3</sub>,<sup>[28]</sup> and *para*-toluenesulfonic acid (*p*-TSA).<sup>[29]</sup> Although these are convenient procedures and give high yields of the desired products, they suffer from one or more drawbacks such as longer reaction time, highly corrosive nature, they involve expensive catalysts, and use solvents. The deprotection of acylals, on the other hand, has also been reported using some of the protic acids such as H<sub>2</sub>SO<sub>4</sub>,<sup>[21]</sup> BiCl<sub>3</sub>,<sup>[30]</sup> Sc(OTf)<sub>3</sub>,<sup>[31]</sup> CAN,<sup>[17]</sup> ZrCl<sub>4</sub>,<sup>[32]</sup> and CBr<sub>4</sub>.<sup>[33]</sup> Most of them are corrosive, expensive, or non-reusable catalysts; hence, developing a more efficient, economical, and greener protocol is still required.

After acknowledging the advantages of solid-supported catalysts, we herein report the use of silica chloride in the synthesis of 1,1-diacetates by a solvent-free reaction of aldehydes with acetic anhydride and their deprotection using silica chloride in the presence of methanol (Scheme 2). Our system takes care of all the problems encountered with the previously mentioned catalysts.



**Scheme 2.** Protection and deprotection of aldehydes using acetic anhydride in the presence of silica chloride.

**Table 1.** Conversion of anisaldehyde (1 mmol) to 1,1-diacetoxy-1-(4-methoxyphenyl) methane in the presence of silica chloride in different solvents and under solvent-free conditions

Entry	Solvent	Yield <sup>a</sup> (%)	Time (min)
1	THF	80	20
2	DCM	62	20
3	Ether	60	20
4	Acetonitrile	80	20
5	Solvent-free reaction	95	15

<sup>a</sup>Isolated yield.

## RESULTS AND DISCUSSION

Synthesis of acylals from aldehydes and acetic anhydride in the presence of *p*-TSA has already been reported from our laboratory.<sup>[29]</sup> The reactions were carried out at room temperature for the protection of aldehydes, whereas deprotection required microwave irradiation. In continuation with our work on protection and deprotection of aldehydes, herein we report a solvent-free synthesis of acylals from aldehydes and acetic anhydride using silica chloride as a catalyst. The catalyst can be filtered and reused for two more runs.

In an initial endeavor, we tried to convert anisaldehyde (1 mmol) to the corresponding acylal in the presence of various solvents and also under solvent-free condition, and as shown in the Table 1 the solvent-free reaction gave the best results. For solid aldehydes (Table 2), 2.5 mmol of acetic anhydride was used to obtain the best results. To test the applicability of our method, we prepared a series of acylals from different aldehydes, and the data shown in Table 2 clearly indicate that electron-withdrawing and electron-donating groups do not have much effect on the yield of the product.


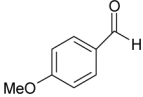
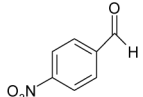
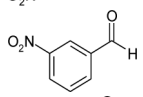
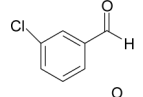
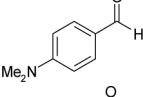
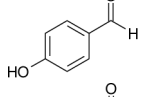
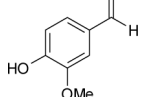
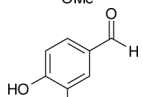


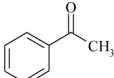
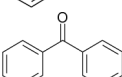
After the protection, the next step comes is deprotection. In a control experiment, 1,1-diacetoxy-1-(4-methoxyphenyl) methane (1 mmol) was taken, and catalytic amounts of silica chloride were added in the presence of methanol. After 40 min, we obtained the anisaldehyde back in good yield.

To check the chemoselectivity of this reaction, a mixture of benzaldehyde (1 mmol) and acetophenone (1 mmol) was added to acetic anhydride (4 mmol) in the presence of silica chloride and stirred at 26–28 °C for 20 h (Scheme 3). Benzaldehyde was converted to acylals, but acetophenone remained as such. This showed that only aldehydes could be selectively converted to geminal diacetates in the presence of keto groups.

## EXPERIMENTAL

All aldehydes were commercial products and were used without further purification. The catalyst silica chloride was prepared as per a reported method,<sup>[6]</sup> and acetic anhydride was prepared from sodium acetate and acetyl chloride. Yields refer to yield of isolated products. Melting points and boiling points were measured on a Büchi B-540 apparatus and infrared (IR) spectra were recorded on Nicolet 400D

**Table 2.** Acylation of aldehydes using acetic anhydride in the presence of silica chloride under solvent-free conditions at room temperature

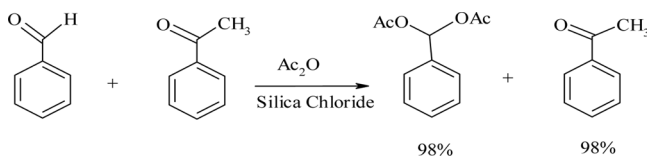
Entry	Substrates	Protection <sup>a</sup>		Deprotection <sup>b</sup>	
		Time	Yield (%) <sup>c</sup>	Time (min)	Yield (%) <sup>c</sup>
a		10 min	98	30	89
b		15 min	95	40	85
c		20 min	94	45	80
d		20 min	92	40	83
e		25 min	90	40	89
f		35 min	86	55	79
g		20 min	95	35	85
h		25 min	90	40	82
i		15 min	95	30	89
j		10 min	90	30	88
k		25 min	91	35	82
l		20 h	ND <sup>d</sup>	—	—
m		20 h	ND	—	—

<sup>a</sup>All the acylals were characterized by comparison of the melting points with authentic samples [Refs. 27, 29] and by the IR spectral analysis.

<sup>b</sup>Deprotection was followed by GC-MS analysis.

<sup>c</sup>Isolated yields.

<sup>d</sup>ND, not detected.



**Scheme 3.** Chemoselective protection of aldehydes.

Fourier transform (FT)–IR Instrument. Gas chromatographic (GC)–mass spectra were obtained using a Shimadzu GC-MS QP 5050A instrument equipped with a 30-m-long and 0.32-mm-diameter BP-5 column with the column temperature 80–150–250 °C.

### General Procedure for the Protection of Aldehydes

Silica chloride (200 mg) was added to a solution of aldehyde (10 mmol) and acetic anhydride (15 mmol) and stirred at room temperature (for a stipulated time as indicated in Table 2). The reactions were monitored by thin-layer chromatography (TLC; ethyl acetate–light petrol 1:9). After completion of the reaction, ether (15 mL) was added, and the catalyst was recovered by filtration. The filtrate was washed with saturated NaHCO<sub>3</sub> solution (10 mL) followed by water (10 mL) and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The filtrate was concentrated under vacuo to get almost pure 1,1-diacetate. Further purification was done by silica-gel column chromatography.

### General Procedure for the Conversion of Acylals into Aldehydes

A mixture of 1,1-diacetate (10 mmol), methanol (5 mL), and silica chloride was stirred at room temperature (for the time indicated in Table 2). TLC (ethyl acetate–light petrol 1:9) was used to monitor the reaction. After completion of the reaction, the mixture was diluted with ether (15 mL) and the catalyst was filtered, washed with chloroform, and reused. The filtrate was washed with brine solution (15 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The filtrate was concentrated and the product was purified by silica-gel column chromatography.

## CONCLUSION

In conclusion, we have explored silica chloride as one of the most versatile, cost-effective, and reusable catalysts for the synthesis of 1,1-diacetates under solvent-free condition and then deprotection of the same to aldehydes in methanol as solvent. The advantages of our protocol are excellent yields, shorter reaction time, and use of ecofriendly catalyst. The present method, in our opinion, is as efficient as our previously reported method.<sup>[29]</sup>

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