

Acetalization of Carbonyl Compounds by Using $\text{Al}_2(\text{HPO}_4)_3$ under Green Condition Mg HPO_4

Fariba Jafari, Samaneh Heydarian

Abstract— $\text{Al}_2(\text{HPO}_4)_3$ was easily prepared and used as a solid acid in acetalization of carbonyl compounds at room temperature and under solvent-free conditions. The protection was done in short reaction times and in good to high isolated yields. The cheapness and availability of this reagent with easy procedure and work-up make this method attractive for the organic synthesis.

Keywords—Acetalization, acid catalysis, carbonyl compounds, green condition, protection.

I. INTRODUCTION

SOLID acids have many advantages such as simplicity in handling, decreasing reactor and plant corrosion problems, and environmentally safe disposal [1]. Also, wastes and by-products can be minimized or avoided by developing cleaner synthesis routes. On the other hand, any reduction in the amount of sulfuric acid needed and/or any simplification in handling procedures is required for risk reduction, economic advantage and environment protection.

Very recently, we among many others have demonstrated that heterogeneous reagent systems have many advantages such as simple experimental procedures, mild reaction conditions and minimization of chemical wastes as compared to the liquid phase counterparts [2]. Thus, inorganic acidic salts such as $\text{Al}_2(\text{HPO}_4)_3$ [3] or $\text{Zr}(\text{HSO}_4)_2$ [4] could be recommended for the above mentioned purposes. Some chemists found that many reactions proceed efficiently in the solid state. Indeed, in many cases, solid state organic reaction occurs more efficiently and more selectively than does its solution counterpart. The solvent-free reaction has many advantages such as reduced pollution, low cost, process simplicity and easier work-up. These factors are especially important in industry.

Acetals are not only the most widely used protecting groups but are also efficient chiral auxiliary groups for enantioselective synthesis [5]. The most convenient and practical method for acetalization is the reaction of carbonyl compounds with ethylene glycol in the presence of an appropriate catalyst. There are some reported in the literature for application of some catalysts for this purpose such as, tetrabutylammonium tribromide, [6] polymer bounded metal complexes, [7] SbCl_3 , [8] silica gel supported metallic sulfates, [9] lithium triflate, [10] polyaniline supported

phosphoric acid salts are usually utilized as solid acid catalysts [11].

Some heterogeneous methods for organic synthesis have been described either a solid acid as catalyst or a supported catalyst. These solids are readily separable from the product by simple filtration and they are recyclable.

In addition, this is a current research and general interest in heterogeneous systems in industry and in developing technologies [12].

In the past two years, utilization of a solid organic acid, sulfamic acid, in catalytic and organic reactions as an alternative for conventional acidic materials have received much attention due to its unique characters nonvolatile, no hygroscopic, odorless, and with crystalline solid with outstanding stability [13]-[17].

We recently reported the tetrahydropyranlation of hydroxy compounds [18], acetolysis of cyclic ethers [19], esterification of cyclic olefin with aliphatic acids under solvent free condition [20] the Beckmann rearrangement of ketoxime in dried CH_3CN [21] and transesterification of ketoester in ionic liquid [22]. We further report here a partial procedure for protection of various carbonyl compounds by the formation of acetals or ketals in the presence of catalytic amount of sulfamic acid.

In conclusion, the carbonyl were efficiently converted to the corresponding dimethyl acetals at room temperature using trimethyl ortho formate as water scavenger and decaborane as a Lewis acid catalyst under a nitrogen atmosphere.

The advantage of this methodology is that it is simple, mild and efficiently de-protected to the corresponding carbonyls using a catalytic amount of decaborane in aqueous THF [23]-[25].

Catalytic technologies have played a vital role in the economic development of the chemicals industry in the 20th century, with a total contribution of ~20% of world GNP. In the 21st century, we can expect the drive toward cleaner technologies brought about by public, legislative, and corporate pressure to provide new and exciting opportunities for catalysis and catalytic processes [26].

A rapidly growing area of heterogeneous catalysis is for environmental pollution control. Although heterogeneously catalyzed processes are widely used in large scale petrochemical processes, the majority of fine, specialty, and pharmaceutical chemicals manufacturing processes rely on homogeneous reagents and catalysts, with solid catalysts used in little beyond hydrogenations. Many of these processes were developed about 100 years ago and had been developed

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simply to maximize product yield, disregarding the environmental impact of inorganic waste and toxic byproducts formed during the reaction. Most of the waste is generated during the separation stage of the process when a typical water quench and neutralization (for acidic or alkaline systems) results in the formation of large volumes of hazardous waste. [26], [27] Increasing waste disposal costs are adding to the environmental costs and the societal costs of an increasingly hostile public toward chemical waste [28], [29].

The efficient use of solid catalysts and reagents that stay in a phase separate from the organic compounds can go a long way to achieving these goals. Product isolation is simplified and reactions often run under milder conditions and give higher selectivity. The atom efficiency of the reaction is improved, the process is simplified, precious raw materials used in the manufacture of the catalyst are given increased lifetime (through reuse), and the volume of waste is significantly reduced. Polymer-supported catalysts have been widely used in research and in process chemistry, but their use is restricted due to easy damage to the organic polymer (thermal or chemical) [30].

Zeolites have excellent thermal and chemical stability and have been incredibly successful in vapor phase chemistry, but they are less useful for many organic reactions in which molecular sizes can exceed the small zeolitic pores and where liquid-phase reactions can lead to diffusion control. We have sought to exploit the recent emergence of mesoporous solids in organic synthesis by designing materials that can accommodate most organic molecules and have active surfaces that can catalyze important reactions [31]. By combining this with innovative engineering appropriate for smaller volume heterogeneous reactions, we hope to develop a range of novel greener processes for the manufacture of higher volume organic chemicals. [32], [33].

Solid acids can be described in terms of their Brønsted/Lewis acidity, the strength and number of these sites, and the morphology of the support (typically in terms of surface area and porosity). High product selectivity can depend on the fine-tuning of these properties. Thus, some rearrangement reactions require pure Lewis acidity. Friedel-Crafts reactions can require Lewis acidity (e.g., for alkylations using alkyl halides) or Brønsted acidity (e.g., for alkylations using alcohol), or indeed, a combination of both (e.g., for Friedel-Crafts acylations using acid chlorides). Pore constraints may influence product selectivity as a result of the sizes of substrates, intermediates or products. At a more fundamental level, the use of mesoporous supports has enabled supported reagents and catalysts to be used in reactions of much bulkier substrates than could be considered for microporous (zeolitic) materials. The synthesis of pure Lewis or Brønsted solid acids is a particularly important challenge where some progress has been made.

II. EXPERIMENTAL

A. Review Stage

All compounds were known and spectroscopic data were compared with those of authentic samples and found to be identical [33].

General chemicals such as carbonyl compounds ethylene glycol, and guaiacol glyceryl ether were purchased from Fluka, Merk, and Aldrich chemical companies. Silica bonded sulfuric acid was synthesized according to our previous reported procedure.

The acetalization products were characterized by comparison of their spectral (IR, ¹H NMR) TLC with the authentic samples.

B. Preparation of Aluminum Hydrogen Phosphate

A 50ml 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 aluminum chloride (4.0 g, 40 mmol) was charged in the flask and concentrated phosphoric acid (7.35 g, 40 mmol) was added drop wise over a period of 30 min at room temperature. HCl evolved immediately. After completion of the addition, the mixture was shaken for 30 min, while the residual HCl was eliminated by suction.

The Al₂(HPO₄)₃ (6.46g) was obtained as white gel. The obtained solid acid was mixed by silica gel (6.43g).

C. Preparation of Aluminum Hydrogen Phosphate

A 50ml 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 zirconium chloride (4.0 g, 40 mmol) was charged in the flask and concentrated sulfuric acid (98%, 7.35 g, 40 mmol) was added drop wise over a period of 30 min at room temperature. HCl evolved immediately. After completion of the addition, the mixture was shaken for 30 min, while the residual HCl was eliminated by suction.

The Al₂(HPO₄)₃ (6.48g) was obtained as white gel. The obtained solid acid was mixed by silica gel (6.53g).

D. Preparation of Ring Acetal by Different Types of Diols under Solvent-Free Condition

A mixture of an aldehyde (2mmol) and diols (1mmol) and The Al₂(HPO₄)₃ (6.48g) placed in a mortar was grinded for 5 minutes.

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in high yield.

E. Preparation of Ring Acetal by Ethylene Glycol under Solvent-Free Condition

A mixture of a meta hydroxy benzaldehyde (2mmol) and Ethylene glycol (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes .

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 82 yield.

F. Preparation of Ring Acetal by Ethylene Glycol under Solvent-Free Condition

A mixture of a meta boromo benzaldehyde (2mmol) and Ethylene glycol (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes .

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 94 yield.

J. Preparation of Ring Acetal by Diol under Solvent-Free Condition

A mixture of a benzaldehyde (2mmol) and Diol (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes .

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 85 yield.

H. Preparation of Ring Acetal by Diol under Solvent-Free Condition

A mixture of a para nitro benzaldehyde (2mmol) and Diol (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes .

The reaction progress was followed by TLC.

After completion of the reaction, Hexane (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 85 yield.

K. Preparation of Ring Acetal by Diol under Solvent- Free Condition

A mixture of a para chloro benzaldehyde (2mmol) and Diol (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes .

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 82 yield.

M. Preparation of Ring Acetal by Propane Three Ole under Solvent- Free Condition

A mixture of a three hydroxy benzaldehyde (2mmol) and propane three ole (1mmol) and The $Al_2(HPO_4)_3$ (6.48g) placed in a mortar was grinded from 5 minutes.

The reaction progress was followed by TLC.

After completion of the reaction, Hexan (30 ml) was added and the mixture was filtered. The ring acetal was obtained as pure crystal in % 83 yield.

III. RESULTS AND DISCUSSION

Recently, we have reported the preparation of silica-bound phosphoric acid as a stable acidic reagent and showed its catalytic activity in synthetic methodology (Fig. 1).

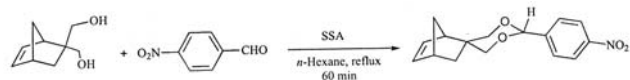


Fig. 1 Catalytic activity of silica-bonded phosphoric acid

Although there are a few reports on the application of inorganic acidic salts such as $Mg(HSO_4)_2$ or $Al(HSO_4)_3$ in synthetic methodology, recently more attention has been paid to the investigation of their potentials in organic synthesis.¹⁴⁻¹⁷ These salts are stable and non-hygroscopic solid material, insoluble in most organic solvents. In continuation of our studies on the application of metallic hydrogensulfate salts in organic synthesis, now we wish to report a convenient method for synthesis of acetals and ketals using $Al(HSO_4)_3$, at room temperature and solvent- free conditions.

Different Kinds of diol a carbonyl compounds were subjected to acetalization reaction in the presence of $Al_2(HPO_4)_3$ at under solvent- free conditions.

As shown in Table I, different class of aldehydes can be efficiently protected as acetal by diols in the presence of $Zr(HSO_4)_2$ under solvent- free condition and pure products were obtained by product extraction by Hexane, simple filtration and solvent evaporation. And Used as of $Al_2(HPO_4)_3$ product yield high.

We hoped that the silica-bond phosphoric acid would be a super reagent to some of the older reported procedures for running acetazation reaction under free solvent condition. AS show in Table I different class of aldehydes can be efficiently protected as acetal by diols in the presence of $Al_2(HPO_4)_3$ under solvent- free condition and pure products were obtained by product extraction by Hexane , simple filtration and solvent evaporation.

In conclusion, an inexpensive and easy procedure for the effective conversion of carbonyl derivatives to their corresponding acetals has been achieved. The cheapness and availability of the catalyst with easy procedure and work-up make this method attractive in organic synthesis. We believe that the present solvent-free methodology would be an important addition to existing methodologies.

Silica bound sulfuric acid can serve as an efficient catalyst for the acetalization of carbonyl compounds under mild and heterogeneous conditions.

The yields are good to excellent and the procedure is simple and convenient. Moreover, the new element here is that the reaction is heterogeneous and this could be worthwhile in an industrial setting for innovative green chemical manufacturing

in the clean work-up and high yield make this method attractive for organic synthesis.

TABLE I
ACETALIZATION OF CARBONYL COMPOUNDS WITH DIOLS BY USING SILICA
SULFURIC ACID UNDER FREE SOLVENT CONDITION

Entry	Diol	Product 1 mmol	Time	Yield%
a			5	82
b			5	94
c			5	85
d			5	82
e			5	82
f			5	83

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