

An Efficient Procedure for Deprotection of Acetals under Mild and Heterogeneous Conditions

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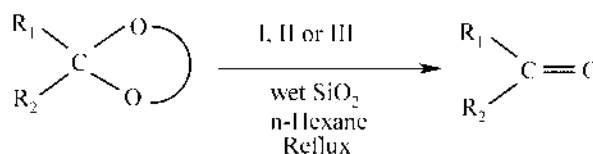
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The electrophilicity of the carbonyl group is a dominant feature of its extensive chemistry. A major challenge in a multistep synthesis is to shield a carbonyl from nucleophilic attack until its electrophilic properties can be exploited. For this reason the protection and deprotection of the carbonyl functional group remain crucial challenges to organic chemists. Experience shows that the critical parameters are generally the stability and the cleavage of the protecting group rather than its introduction. As with most protecting groups, then many methods are available for the deprotection of acetals and ketals. A number of methods have been reported using Vanadyl(IV) Acetate,¹ Cerium(III)Chloride,² Triphenylphosphine/carbon tetrabromide,³ Ferric Chloride Hexahydrate,⁴ Silica Sulfuric Acid,^{5,6} Cu(NO₃)₂·N₂O₄, or Fe(NO₃)₃·1.5N₂O₄,⁷ Pyridinium Poly(hydrogen fluoride),⁸ WCl₆,⁹ γ -Picolinium chlorochromate,¹⁰ Decaborane,¹¹ Benzyl-triphenylphosphoniumperoxo-disulfate,¹² and etc.

Acids are the catalysts which are used the most in industry, including the fields of oil refining, petrochemicals and chemicals. They are responsible for producing more than 1×10^8 mt/year of products. Among the first acid catalysts, the most commonly used were H₂F, H₂SO₄, HClO₄, and H₃PO₄ (in liquid form or supported on Keiselguhr). Solid acids have many advantages such as simplicity in handling, decreasing reactor and plant corrosion problems, and environmentally safe disposal.^{13,14} Also, wastes and by-products can be minimized or avoided by developing cleaner synthesis routes.¹⁵ 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. In addition, there is current research and general interest in heterogeneous systems because of the importance such systems in industry and in developing technologies.¹⁶ 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.²³⁻²⁷ Thus, inorganic acidic salts such as: Al(HSO₄)₃^{17,18} Mg(HSO₄)₂^{19,25} and NaHSO₄·H₂O²³⁻²⁹ could be recommended for above mentioned purposes. Although there are a few



Scheme 1

reports on the application of these salts in synthetic methodology, but only recently, more attention has been paid to the investigation of their potentials in organic synthesis.¹⁷⁻²⁹ Now we wish to report a convenient method for deprotection of acetals or ketals using Al(HSO₄)₃ (**I**), Mg(HSO₄)₂ (**II**) and NaHSO₄·H₂O (**III**) in the presence of wet SiO₂ (Scheme 1).

Results and Discussion

The conversion results of various acetals and ketals to their corresponding carbonyl compounds are presented in Table 1.

The products were isolated simply by filtering the reaction mixture and evaporating the solvent from the filtrate.

As shown in Table 1, the ratio of the amount of reagent to substrate is as follow: Al(HSO₄)₃ < Mg(HSO₄)₂ < NaHSO₄. By surveying of the results, it is clear that Al(HSO₄)₃ is the best one. Meanwhile, the deprotection rate of ketals is more than that of acetals (entry 3, 8, 13 in Table 1). In addition, the presence of an electron releasing group on acetal structure is as a reason for increasing the yield of deprotection (entry 9 and 11 in Table 1).

In conclusion, a cheap and easy procedure for the effective conversion of acetals and ketals to their corresponding carbonyl derivatives has been achieved. The cheapness and availability of the reagents, easy procedure and work-up make this method attractive for the large-scale operation.

Experimental Section

General: Chemicals were purchased from Fluka, Merck and Aldrich chemical companies. Acetals and ketals were synthesized in our laboratory. Deacetalization products were characterized by comparison of their spectral (IR, ¹H-NMR),

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Table 1. Deacetalization of acetals and ketals with $\text{Al}(\text{HSO}_4)_3$ (I), $\text{Mg}(\text{HSO}_4)_2$ (II), or $\text{NaHSO}_4 \cdot \text{H}_2\text{O}$ (III) in the presence of Wet SiO_2 under mild and heterogeneous condition

Entry	Substrate (A)	Product (B)	I ^a Time (min)/ ^d Yield (%)	II ^b Time (min)/ ^d Yield (%)	III ^c Time (min)/ ^d Yield (%)
1			60/85	60/79	60/75
2			60/86	50/82	60/80
3			60/85	60/75	60/70
4			60/90	120/85	60/81
5			60/96	60/85	60/84
6			60/95	60/92	60/90
7			60/87	60/85	50/80
8			35/85	60/83	50/80
9			40/90	45/85	45/80
10			60/84	60/70	120/60
11			35/92	30/90	36/80
12			40/90	40/88	60/70
13			60/90	60/85	60/75
14			60/93	60/85	60/70

^a $\text{Al}(\text{HSO}_4)_3$: Substrate: Wet SiO_2 (60%); (1.9 mmol: 1.4 mmol: 0.6 g). ^b $\text{Mg}(\text{HSO}_4)_2$: Substrate: Wet SiO_2 (60%); (2.7 mmol: 1.4 mmol: 0.6 g). ^c NaHSO_4 : Substrate: Wet SiO_2 ; (15 mmol: 1.4 mmol: 3 g). ^disolated yields.

TLC and physical data with the authentic samples.

Deacetalization of the acetal (A11) to Vanillin (B11), a typical procedure: A mixture of the acetal **A11** (1.4 mmole, 0.4 g), *n*-Hexane (15 mL), $\text{Al}(\text{HSO}_4)_3$ (1.9 mmol, 0.6 g) and wet SiO_2 (w/w, 60%, 0.6 g) were refluxed for 35 min.

Reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid residue was washed with dichloromethane. Evaporation of the solvent gave the vanillin **B11**, 0.19 g (92%).

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