

Heteropolyacid catalyzed Synthesis of trimethylsilylethers form alcohols

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Abstract

Synthesis of trimethylsilylethers was carried out using heteropolyacid as solid acid catalyst, variety of alcohols underwent the reaction at room temperature. The reusability of the catalyst has made the protocol simple, cost-effective and environmentally benign. High yields, short reaction time offer added advantage to the protocol.

Keywords Heteropolyacid, trimethylsilylethers, alcohols, protection.

Introduction

With an objective to develop environmentally friendly methods that obviate the need for potentially toxic metal-based catalysts in organic transformations, during the past two decades, there has been a remarkable increase in interest towards the development of new synthetic methodologies employing various non-conventional acid and base catalysts. One particularly useful mode of catalysis is heterogeneous catalysis and catalytic transformations using solid heterogeneous catalysts have received considerable attention within the synthetic organic chemistry community.¹

The use of solid acids as replacement catalysts for conventional Lewis or Bronsted acids in various reactions has attracted a great deal of interest. They have served as important functional materials for petroleum refinery and in the production of fine chemicals.² At present about 200 industrial processes using solid acid catalysts are in operation.³ These industries use acids of type zeolites, metal oxides, mixed oxides, phosphates, heteropolyacids, etc. Solid acid supported reagents based on inexpensive inorganic solids, notably clays and silica also show high promising catalytic activities.⁴⁻⁹

Heteropolyacid is defined as a condensate of different types of oxoacids. In water, all protons of these heteropolyacids are dissociated leaving heteropoly anions having Keggin and Dawson structures. They are represented by a general formula $H_{(8-x)}X M_{12}O_{40}$ where $X = Si^{+4}$, P^{+5} and $M = W^{+6}$ or Mo^{+6} . These materials have very high acidity. as determined using Hammett indicator test.¹⁰ When the stepwise dissociation constants of the heteropolyacids were compared with those of inorganic acids heteropolyacids were proved to be significantly stronger than typical inorganic acids, including H_2SO_4 , HBr , HCl , HNO_3 and $HClO_4$. The

main reason of the strong acidity of HPAs is attributed to the large size and charge of the anions.¹¹

Protection of Hydroxyl Function as Trimethylsilylethers: Hydroxyl group is one of the most versatile group present in a number of organic compounds like nucleosides, alcohols, phenols, carboxylic acids, etc. and its controlled manipulation during the synthesis is of great value to synthetic chemists. As hydroxyl group can undergo acetylation, halogenation, oxidation etc., its protection becomes essential in multi-step organic synthesis. Alcohols are usually protected as their methyl ethers, benzyl ethers, MOM-ethers, THP ethers, trimethylsilyl (TMS) ethers and tert-butyldimethylsilyl (TBDMS) ethers. Amongst these, methyl ethers, benzyl ethers and MOM ethers are quite stable and are difficult to cleave. However, the conversion of alcohols to THP, TMS and TBDMS ethers is preferred for two reasons. i) The deprotection of hydroxyls as THP, TMS and TBDMS ethers can be effected employing simple and mild reaction conditions. ii) Their oxidative deprotection to corresponding carbonyls is also possible. They are preferred only when their use is inevitable. However, TMS ethers are easy to manipulate and are relatively stable. Thus, the protection of hydroxyls as TMS ethers is preferred.

Experimental

The reaction was carried out at room temperature by starting a mixture of alcohol, hexamethyldisilazane (HMDS), catalyst ferric dodecatungstophosphate and dichloromethane as solvent. Upon completion of the reaction (TLC), dichloromethane (10 mL) was added and the catalyst was filtered, washed with dichloromethane (2×5 mL) and from the combined dichloromethane extract the solvent was removed under vacuum. The residue obtained was chromatographed over silica gel (hexane-ethyl acetate, 9:1, v/v) to afford pure product. The different alcohols which underwent the reaction are given in the table below.

Entry	Alcohol	Time (min)	Yield (%)
1	C ₆ H ₅ CH ₂ OH	40	89
2	4 H ₃ CO C ₆ H ₄ CH ₂ OH	30	81
3	4 -Cl C ₆ H ₄ CH ₂ OH	20	93
4	4-H ₃ C C ₆ H ₄ CH ₂ OH	50	85
5	4-(CH ₃) ₂ HCC ₆ H ₄ CH ₂ OH	60	82

6	4-O ₂ NC ₆ H ₄ CH ₂ OH	20	91
7	3,4 (OCH ₃) ₂ C ₆ H ₃ CH ₂ OH	30	89
8	4 NC- C ₆ H ₄ CH ₂ OH	30	87
9	4 (CH ₃) ₂ N C ₆ H ₄ CH ₂ OH	30	88
10	3,4(OCH ₂ O) C ₆ H ₄ CH ₂ OH	60	81

Result and discussion

The general scheme for the protection of alcohols by using heteropolyacid as catalyst and dichloromethane as a solvent is given as follows.



Amongst the large number of silylating agents and methods used for the introduction TMS group on a variety of alcohols¹² Hexamethyldisilazane (HMDS) has been found to be the most convenient to use. This is because, HMDS is inexpensive, easy to handle and is a commercially available reagent. Furthermore, upon silylation, ammonia being the only by-product of this reaction, separation of silylated product is much easier. The principle drawback of HMDS is its poor silylating power which demands either forceful conditions or long reaction times.¹² However, the activity of HMDS can be increased by using a variety of Lewis as well as Bronsted acid catalysts such as H₂SO₄,¹³ chlorotrimethylsilane,^{13a} montmorillonite K-10,^{13b} zinc chloride,^{13c} phosphomolybdic acid,^{13d} tungstophosphoric acid,^{13e} aluminium triflate,^{13f} N, N, N¹, N¹-tetrabromo benzene-1,3-disulfonamide,^{13g} etc. All these methods have their own merits and demerits but they follow the same mechanism^{14,15}. In the present study, we have demonstrated for the first time the usefulness of a commercially available and inexpensive ferric dodecatungstophosphate as an efficient, heterogeneous, solid acid catalyst for effect protection of alcohols as trimethylsilylethers.

The present protocol typically circumvents the drawbacks associated with the many of the earlier reported protocols.

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