

Acetyl-Tethering Silica as a Novel Reagent for Acetylation of Alcohols under Mild and Heterogeneous Conditions

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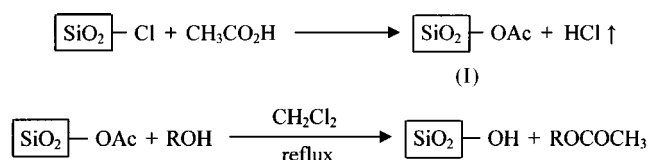
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During the multistep synthesis of natural products, the efficiency of the synthetic protocol employed often depends largely on protection and deprotection of functional groups involved. To this end, protecting groups have been playing a crucial role during the synthesis of complex natural products.¹ Among the various protecting groups used for hydroxyl function, acetyl is the most common group in view of its easy introduction, stability to acidic reaction conditions and also ease in its removal by mild alkaline hydrolysis. Acetylation is normally performed by using acetic anhydride or acetyl chloride in the presence of a base such as triethylamine or pyridine. Further, the rate of acetylation is known to be increased manifoldly if 4-dimethylaminopyridine is used as a co-catalyst.² *p*-Toluenesulfonic acid³ (a protic acid) and Lewis acids such as TiCl₄/AgClO₄,⁴ CoCl₂,⁵ Cu(OTf)₂,⁶ Sc(OTf)₃,⁷ TaCl₅,⁸ MgBr₂,⁹ FeCl₃,¹⁰ Cu(NO₃)₂·3H₂O¹¹ have been used to acetylate alcohols. Apart from these catalysts, TMSOTf,¹² and TMSCl¹³ have been used as efficient catalysts for acetylation of alcohols. There have been efforts to introduce solid reagents for easier work-ups. In this regard montmorillonite K-10,^{14,15} KSF,¹⁵ Zeolite HSZ-360,¹⁶ and KF-Al₂O₃¹⁷ have been used.

In continuation of our studies on the applications of chloride-tethering,^{18,19} we found that chloride-tethering silica²⁰ in reaction with glacial acetic acid can be converted



Scheme 1

easily to the acetyl-tethering silica (I). It is interesting to note that the reaction is easy and clean, not requiring any complex work-up procedure because the evolved HCl gas can be removed from the reaction vessel immediately. We believed that acetyl-tethering silica would be a superior acyl source, therefore we were interested in using this resin for acetylation of alcohols (Scheme 1). All reactions were performed under mild and heterogeneous conditions in refluxing dichloromethane. The results are tabulated in Table. Formation of the mixture of the products, causes that this methodology can not be used for the acetylation of allylic alcohols (Table 1, Entry 11).

In conclusion, acetyl-tethering silica is a good acyl source in terms of convenience, cheapness, easy production and insolubility in organic solvents. Practical and efficient acetylation of alcohols were achieved by the present methodology. The cheapness and availability of the reagents, easy procedure and work-up make this method attractive

Table 1. Acetylation of alcohols with acetyl-tethering silica in refluxing dichloromethane

Entry	Substrate	Time (hr)	Product	Yield% ^{a,b}
1	4-ClC ₆ H ₄ CH ₂ OH	1	4-ClC ₆ H ₄ CH ₂ OAc	90
2	2-ClC ₆ H ₄ CH ₂ OH	1.5	2-ClC ₆ H ₄ CH ₂ OAc	93
3	4-BrC ₆ H ₄ CH ₂ OH	1	4-BrC ₆ H ₄ CH ₂ OAc	92
4	2-BrC ₆ H ₄ CH ₂ OH	1	2-BrC ₆ H ₄ CH ₂ OAc	95
5	2-NO ₂ C ₆ H ₄ CH ₂ OH	2	2-NO ₂ C ₆ H ₄ CH ₂ OAc	85
6	2-CH ₃ C ₆ H ₄ CH ₂ OH	1	2-CH ₃ C ₆ H ₄ CH ₂ OAc	90
7	C ₆ H ₅ CH(OH)CH ₃	1.5	C ₆ H ₅ CH(OAc)CH ₃	87
8	C ₆ H ₅ CH ₂ CH ₂ CH ₂ OH	1.5	C ₆ H ₅ CH ₂ CH ₂ CH ₂ OAc	85
9	C ₆ H ₅ CH ₂ CH(OH)CH ₃	1.5	C ₆ H ₅ CH ₂ CH(OAc)CH ₃	90
10	Cyclohexyl-OH	1.5	Cyclohexyl-OAc	80
11	C ₆ H ₅ CH=CHCH ₂ OH	3	C ₆ H ₅ CH=CHCH ₂ OAc	— ^c

^aProducts were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy, ^bIsolated yields, ^cMixture of products.

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for the large-scale operations. The other importance of this methodology is the regeneration of silica gel which can be used for the preparation of chloride-tethering silica and acetyl-tethering silica for several times. Moreover, a new feature here is the fact that the reaction is heterogeneous. This could be worthwhile in an industrial setting.²¹

Experimental Section

Preparation of acetyl-tethering silica: To chloride-tethering silica (2 g) in 50 mL suction flask which was equipped with a gas inlet tube for conducting HCl gas over an adsorbing solution *i.e.* water and a drying tube was added glacial acetic acid (10 mL) and shaken for 1 hr. The mixture was filtered and the white solid residue was washed with acetone (5 mL), and stored in a tightly capped bottle, [IR (KBr): 1620, 1200, 1060 cm⁻¹].

General procedure: A mixture of the substrate (1 mmol) and acetyl-tethering silica (0.6 g) in dry dichloromethane (5 mL) was heated at reflux for the specified time (Table 1). The reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the filtrate was washed with dichloromethane (10 mL). Evaporation of the solvent gave the corresponding esters in good to high yields.

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