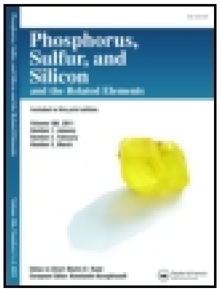

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SILICA CHLORIDE AS A MILD AND EFFICIENT REAGENT FOR ACETYLATION OF ALCOHOLS

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A variety of alcohols underwent acetylation with acetic anhydride in the presence of silica chloride. All reactions were performed at room temperature and under completely heterogeneous conditions in good to high yields.

Keywords: Acetylation; alcohol; esterification; heterogeneous conditions; silica chloride

Functional group protection and deprotection is important in synthetic organic chemistry.[1] Among protecting groups for alcohols, the esters are the most important with acetate being the simplest and easiest of all. Acetylation[2] most commonly is performed using[3,4] reagents such as acetic anhydride or acetyl chloride in the presence of triethyl amine or pyridine as a catalyst.[5] 4-(Dimethylamino)pyridine (DMAP) is known to increase the rate of acetylation when used as a cocatalyst.[6]

Tributylphosphine has been introduced as a less basic catalyst for acetylation of alcohols.[7] In addition to the above catalysts, protic or Lewis acids,[8–14] or some times solid acid catalysts[15–17] are known to catalyze the acetylation of alcohols with acid anhydrides. Recently, scandium triflate has been used for the efficient acetylation of alcohols.[18] Most recently, the use of bismuth as a milder acetylation catalyst than scandium triflate has been reported.[19] However most of the reported methods suffer from one or more of the following disadvantages: long rection time, vigorous reaction conditions, the occurance of side

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reactions, unavailability of the reagents, as well as poor yields of the desired product. Thus, there still is a demand to develop new and mild methods for the acetylation of alcohols in the presence of inexpensive and bench top reagents.

Silica chloride has been used as a mild and efficient reagent for a number of organic reactions.[20–22] In this article we disclose a new method for the acetylation of alcohols using acetic anhydride in the presence of silica chloride in n-hexane (Scheme 1).

$$\mathrm{ROH} \xrightarrow[\text{n-hexane, r.t., 5–30 min.}]{(\mathrm{CH_3CO})_2\mathrm{O},\ \text{silica chloride}} \mathrm{ROCOCH_3}$$

SCHEME 1

As shown in Table I, primary and secondary alcohols are acetylated with acetic anhydride in excellent yields in the presence of silica chloride (entries 1–15). Dihydroxy compounds are converted into the corresponding diacetates efficiently (entry 16). Interestingly, hindered

TABLE I Acetylation of Alcohols Using Ac_2O in the Presence of Silica Chloride[a]

Entry	Substrate	Product	Time (min.)	Yield %[b]
1	$C_6H_5CH_2$ OH	$C_6H_5CH_2$ OAc	5	90
2	2-$BrC_6H_4CH_2$ OH	2-$BrC_6H_4CH_2$ OAc	5	86
3	4-$MeOC_6H_4CH_2$ OH	4-$MeOC_6H_4CH_2$ OAc	5	85
4	4-$ClC_6H_4CH_2$ OH	4-$ClC_6H_4CH_2$ OAc	5	85
5	4-$(Me)_3CC_6H_4CH_2$ OH	4-$(Me)_3CC_6H_4CH_2$ OAc	3	90
6	3-$NO_2C_6H_4CH_2$ OH	3-$NO_2C_6H_4CH_2$ OAc	5	85
7	$C_6H_5CH(OH)CH_3$	$C_6H_5CH(OAc)CH_3$	5	92
8	$C_6H_5CH(OH)C_6H_5$	$C_6H_5CH(OAc)C_6H_5$	15	88
9	$C_6H_5CH{=}CHCH_2$ OH	$C_6H_5CH{=}CHCH_2$ OAc	5	85
10	$C_6H_5CH_2CH(OH)CH_3$	$C_6H_5CH_2CH(OAc)CH_3$	10	85
11	$C_6H_5CH_2CH_2CH_2$ OH	$C_6H_5CH_2CH_2CH_2$ OAc	5	80
12	Cyclohexanol	Cyclohexyl acetate	5	85
13	1-octanol	1-octyl acetate	2	82
14	1-butanol	1-butyl acetate	10	80
15	(−) menthol	(−) menthyl acetate	10	86
16	$C_6H_5CH(OH)CH_2OH$	$C_6H_5CH(OAc)CH_2OAc$	12	82[c,d]
17	*tert*.butyl alcohol	*tert*.butyl acetate	30	85
18	1-methylcyclohexanol	1-methylcyclohexyl acetate	10	80

[a] Products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy.

[b] Isolated yield.

[c] Yield refers to isolated pure diacetate.

[d] 2.5 mmol of acetic anhydride was used.

tertiary alcohols such as *tert*-butyl alcohol and 1-methylcyclohexanol (entries 17 and 18) also are acetylated in excellent yields in the presence of this reagent. The acetylation reactions were performed under mild and completely heterogeneous conditions at room temperature and take place with good to high yields.

In conclusion, we have shown that silica chloride is a very efficient and versatile reagent for acetylation of alcohols. One of the advantages of this method is that even hindered substrates can be acetylated in high yields under mild reaction conditions. The actual role of silica chloride is not clear and this subject is under investigation in our laboratory.

EXPERIMENTAL

General Procedure for Acetylation of Alcohols Using Ac_2O in the Presence of Silica Chloride[23]

A mixture of alcohol (1 mmol), acetic anhydride (1.5 mmol), and silica chloride (0.1 g) in n-hexane (3 mL) was stirred at room temperature for the specified time. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, the solvent was evaporated and water was added (10 mL). The mixture was extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was separated, washed with saturated $NaHCO_3$ (2 × 10 mL) and water (10 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by column chromatography on silica gel afforded the pure acetate.

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