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An atom-efficient and powerful method for direct esterification of silyl ethers catalyzed by $HClO_4-SiO_2$

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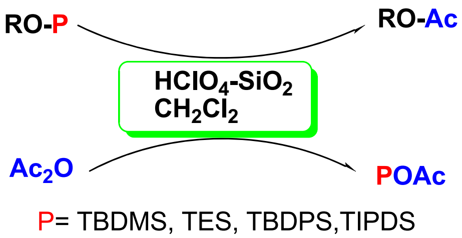
ABSTRACT

An efficient and convenient procedure for direct esterification of alkyl and aryl silyl ethers with Ac_2O and a catalyst system of perchloric acid immobilized on a silica gel ($HClO_4-SiO_2$) has been developed. The silyl protecting groups are directly replaced by acetyls and the protecting groups themselves are transformed into acetates as the sole byproducts, which can be readily recovered and converted back to silylchlorides, the original protecting agents, thus minimizing wastes.

1. Introduction

Green chemistry advocates the need for environmentally benign synthesis, which incorporates high atom efficiency, diminishes or eliminates in the use or generation of hazardous reagents or wastes and the cyclic use of reagents and catalysts.[1] In most cases, protecting groups are indispensable in the multistep synthesis of natural products and medicinal compounds but are the antithesis of atom economy.[2] Silyl groups are the most frequently employed hydroxy protecting group. In the presence of Lewis or protic acids, however, they are labile.[2a,3] On the other hand, esters are quite stable to Lewis and protic acids. The different stability of these two kinds of protecting group often necessitates changing one or more protecting groups.[4] Direct transformation presents an obvious advantage for this purpose as it replaces two steps: cleavage of the primary protecting group(s) and the subsequent installation of the new protecting group(s). Therefore, studies in synthetic methods for direct transforming protecting groups are considered valuable.[5]

A number of methods have been reported for the transformation of *tert*-butyldimethylsilyl (TBDMS) ethers to acetates, using $FeCl_3-Ac_2O$,[6] $Cu(OTf)_2-Ac_2O$,[7] $In(OTf)_3-Ac_2O$,[8] $AcBr-SnBr_2$,[9] $AcCl-ZnCl_2$,[10] $TiCl_4-Ac_2O$,[11] $ZrCl_4-Ac_2O$,[12] or $BF_3\cdot Et_2O-NaI-Ac_2O$.[13] Each of these methods is incompatible with some functional groups or delicate structures, limiting their application. This laboratory has found that the $FeCl_3-Ac_2O$ combination induces undesired pentofuranose and pentofuranoside chain-opening.[14] Moreover, the high cost and susceptibility to moisture would be a major concern in the industrial applications of a metal salt. The presence of a metal halide also leads to a tedious workup when conducted on large scales.[15] Therefore, a mild, effective, and environmental benign procedure for this purpose would be of value and is still required for green organic synthesis. This report describes an effective and environmental-friendly protocol for direct conversion of silyl ethers into acetates in the presence of $HClO_4-SiO_2$ (Scheme 1), a catalyst, which is readily recovered and reused.[16]



Scheme 1. Direct transformation of silyl ethers to acetates.

2. Results and discussion

2.1. Direct esterification of alkyl silyl ethers

With the concept of waste minimization in mind, we have developed a method for direct transformation of acetonide into acetates using an $Ac_2O-HClO_4-SiO_2$ system.[17] Under the same conditions, the

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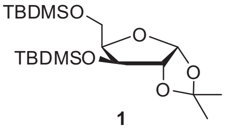
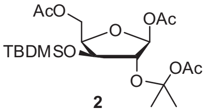
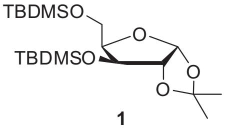
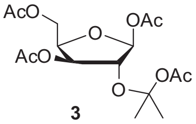
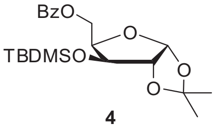
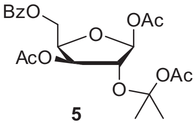
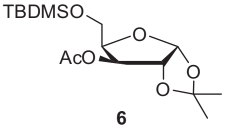
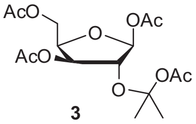
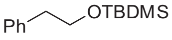
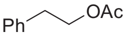
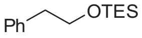
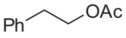
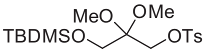
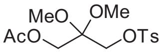
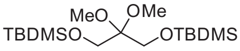
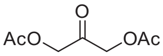
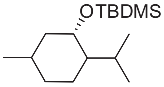
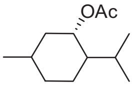
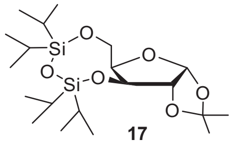
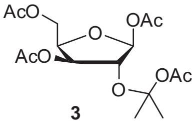
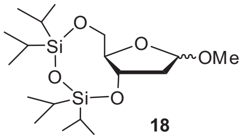
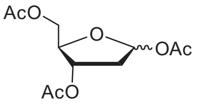
primary TBDMS group in **1** was readily displaced by an acetyl group to give **2** in 94% isolated yield (entry a, Table 1). Furthermore, under reflux in CH_2Cl_2 solution, both TBDMS groups were simultaneously substituted to afford **3** in 89% isolated yield (entry b, Table 1). Encouraged by these results and mild reaction conditions without the use of metal salts, the scope of this protocol was examined further. The steric hindered secondary ether **4** was transformed smoothly under reflux conditions to afford the desired product **5** in 87% isolated yield. Both primary TBDMS ethers **6** and **7** were also successfully transformed at rt (entry d and e, Table 1). In all cases as described above, the anomeric acetonide group was transformed into an open-chain isopropylidene acetal similar to the results obtained as transformation of acetonides.[14,17a] As anticipated, displacement of the TES ether in **9** was more readily achieved as the triethylsilyl (TES) ethers are much more sensitive to acid than TBDMS ethers.[2a,3a]

Moreover, using this one-pot procedure, selective transformation of TBDMS ethers of **11** was successfully achieved without affecting the acid labile dimethyl acetal group (entry g, Table 1).

Table 1
Direct transformation of alkyl silyl ethers into acetates catalyzed by $HClO_4–SiO_2$

Entry	Substrate	Product	Time (h)	Yield[a] (%)
a	 **1**	 **2**	0.5	94[17a]
b	 **1**	 **3**	2 (Reflux)	89[17a]
c	 **4**	 **5**	2 (Reflux)	87[17a]
d	 **6**	 **3**	0.5	89[17a]
e	 **7**	 **8**	0.75	91
f	 **9**	 **8**	0.5	89
g	 **11**	 **12**	2	85
h	 **13**	 **14**	3	81
i	 **15**	 **16**	1 (reflux)	91
j	 **17**	 **3**	5 (reflux)	87
k	 **18**	 **19**	4 (reflux)	84[18]

[a] Isolated yields and reproduced at least twice for each cases.