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ACTIVATION AND SYNTHETIC APPLICATIONS OF THIOSTANNANES. CHEMICAL MODIFICATION OF HYDROXY FUNCTION UNDER PROTECTION

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Abstract. Tetrahydropyranyl ethers are converted in one-pot into benzyl and α-methoxyethoxymethyl ethers, benzoates, tosylates, and aldehydes on treatment with thiostannanes in the presence of $BF_3{\cdot}OEt_2$ followed by exposure of the resulting alkoxystannanes to electrophiles or PCC.

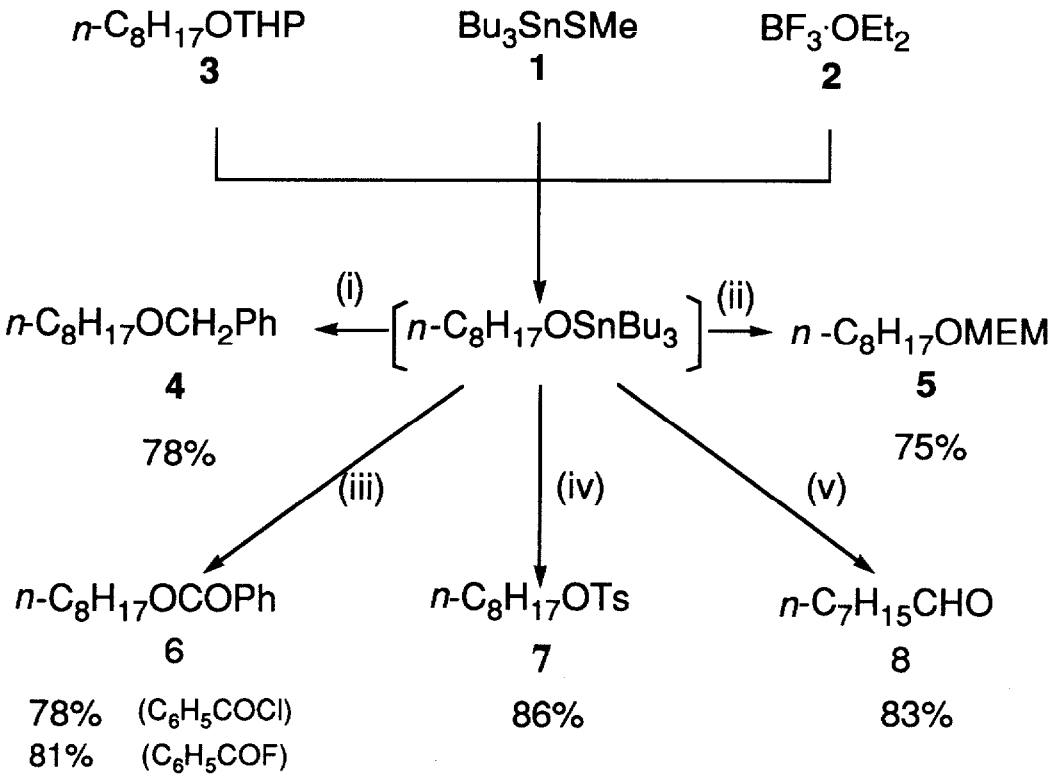
Protection of functional groups is an unavoidable process in organic synthesis.[1] A protective group is removed after completion of required manipulations on a molecule, and the parent functional group thus regenerated undergoes further desired modifications. It is therefore of great synthetic value if a protected functional group could be transformed without passing through intermediary unmasked stages into other types of protected forms or functionalities. This, however, opposes *the original sence of protection* which means deactivation of labile groups. Nontheless, there have appeared a few examples, though in somewhat limited manner, belonging to this category.[2,3] Here we wish to report a versatile method for one-pot transformation of tetrahydropyranyl (THP) ethers, the most important protective form of hydroxy groups, into various functionalities.

Previously, we reported that thiostannanes combined with $BF_3{\cdot}OEt_2$ effected thioalkoxylation of acetals giving monothioacetals exclusively;[4]

$$RR'C(OR")_2 + Bu_3SnSPh \xrightarrow{BF_3{\cdot}OEt_2} RR'C(OR")(SPh) + Bu_3SnOR"$$

Quite reasonably we can assume alkoxystannanes to be formed as the counterpart in the products in this reaction. Our basic idea of the present study stemmed from that in-situ utilization of the alkoxystannanes formed in this thioalkoxylation should allow us to conduct versatile functional group modifications under mild conditions since alkoxystannanes have found a number of synthetically useful reactions.[5] This is indeed the case as illustrated in Scheme 1. To a toluene solution of *n*-C_8H_{17}OTHP (**3**) were added Bu_3SnSMe (**1**) (1.1 equiv) and $BF_3{\cdot}OEt_2$ (**2**) (1.1

Scheme 1

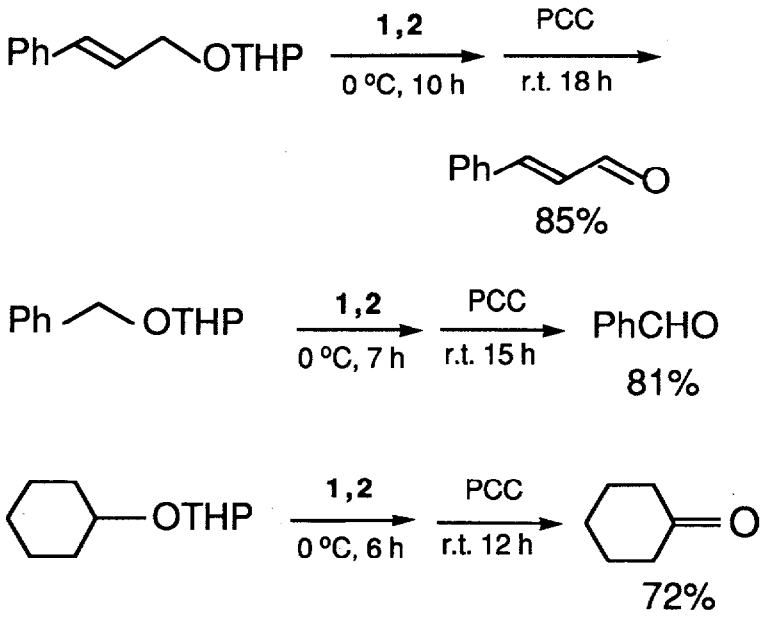


(i) $C_6H_5CH_2I$(1.3 equiv), CsF (1.3 equiv), DMF, MS 3A, r.t., 20 h. (ii) MEMCl (3.5 equiv), CsF (1.5 equiv), DMF, MS 3A, r.t., 12 h. (iii) C_6H_5COCl (2.5 equiv) or C_6H_5COF (2.5 equiv), $CHCl_3$, MS 3A, r.t., 70 h. (iv) *p*-$CH_3C_6H_4SO_2Cl$ (2.0 equiv), $CHCl_3$, MS 3A, 40 °C, 70 h. (v) PCC (2.0 equiv), CH_2Cl_2, MS 3A, r.t., 10 h.

equiv) at 0 °C, and the solution was stirred for 7 h. Then, the solvent was replaced by DMF. To this solution were added benzyl iodide (1.3 equiv), CsF (1.3 equiv), and molecular sieves (MS) 3A.[6] The reaction mixture was stirred for 20 h at room temperature. Usual workup provided benzyl octyl ether (**4**) in 78% yield. Employment of 2-methoxyethoxymethyl (MEM) chloride (3.5 equiv) in place of benzyl iodide furnished the MEM ether **5** in 75% yield. Exposure of the initial reaction mixture containing the octyloxystannane to benzoyl chloride in chloroform delivered the benzoate **6** in 78% yield. In the case where separation of resulting tributyltin chloride and the benzoate is not easy, benzoyl fluoride is preferably employed since tributyltin fluoride is more easily separated from the reaction mixture. The tosylate **7** was obtained in 86% yield by use of *p*-toluenesulfonyl chloride. Finally, oxidation with pyridinium chlorochromate (PCC) in dichloromethane led to octanal (**8**) in 83% yield.

Scheme 2 shows that allylic, benzylic, and secondary alkyl THP ethers are available.

Scheme 2



1-Octanol was subjected to analogous benzylation and tosylation in the absence of the thiostannanes. No reaction occurred at all even after prolonged reaction time. These results support our premise of the initial formation of alkoxylstannanes. In this sence, the THP group operates not only as a simple protective group but also as an activator of a hydroxyl function.

$$n\text{-}C_8H_{17}OH + C_6H_5CH_2I + \mathbf{2} + CsF + MS\ 3A \xrightarrow[DMF,\ r.t.\ 72\ h]{} \text{No Reaction}$$

$$n\text{-}C_8H_{17}OH + p\text{-}CH_3C_6H_4SO_2Cl + \mathbf{2} + MS\ 3A \xrightarrow[CHCl_3,\ r.t.\ 67\ h]{} \text{No Reaction}$$

In summary, we have established one-pot conversion of acetal protection into various functionalities under mild reaction conditions. The present method obviously meets a wide spectrum of synthetic demands. Of course, hydroylsis of the intermediary alkoxystannanes regenerates the parent alcohols. This new deprotection method will be described in detail in a full account.

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(3) We don't classifiy transesterifcation and -acetallization into this category since they are simple exchange reactions and involve no activation or modifiaction of functionalities.

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