# *Communications*

## Distannoxane-Catalyzed Highly Selective Acylation of Alcohols

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Acylation of alcohols has enjoyed constant renovation due to its significance in synthetic chemistry. Acetic anhydride is the most frequently employed reagent. Probably, the first practical breakthrough in this technology was brought about by the discovery of the 4-(dialkylamino)pyridine catalysts.[1] Further improvements have been advanced in the relevant studies.[2] More recently, a variety of new catalysts appeared that are either basic or acidic. $Bu_3P$,[3] $MgBr_2-R_3N$,[4] and an aminophosphine superbase[5] fall in the former category, while $Sc(OTf)_3$[6] and $TiCl(OTf)_3$[7] fall in the latter. 3-Acetylthiazolidine-2-thiones-NaH[8] and AcCl-hindered amine[9] were employed for selective acylation of primary alcohols.

Transesterification is another important means, but unfortunately, it is difficult to reach high conversions with this reaction due to its reversibility.[10] This drawback can be overcome by using enol esters that are capable of escaping from the equilibrium because of their conversion into aldehydes or ketones upon transesterification. This reaction is usually conducted under acidic conditions.[11] Recently, $Cp^*_2Sm(thf)_2$ or $SmI_2$ was found to be effective, yet this method required the Schlenk tube technique.[12]

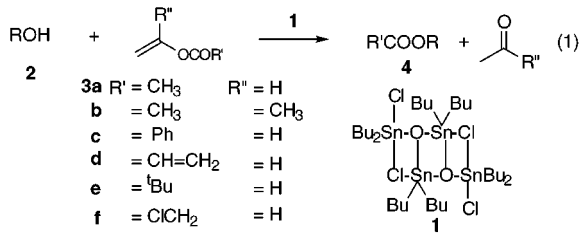
Previously, we disclosed that 1,3-disubstituted tetraalkyldistannoxanes that have a dimeric formulation like **1** catalyzed transesterification under virtually neutral conditions.[13,14] Therefore, we expected that distannoxane-catalyzed transesterification, when coupled with the enol ester protocol, would give rise to a new practical method for acylation of alcohols. This is indeed the case. We report herein a convenient way for the highly selective acylation of alcohols that is difficult to achieve with other catalysts.

**Table 1. Distannoxane-Catalyzed Acylation of Alcohols[a]**

| entry | 2 | 1[b] (mol %) | 3 | condns (°C, h) | 4[c] (% yield) |
|---|---|---|---|---|---|
| 1 | $C_8H_{17}OH$ (**2a**) | 1 | **3a** | 30, 24 | 99 |
| 2 | **2a** | 5 | **3a** | 30, 5 | 93 |
| 3 | **2a** | 1 | **3a** | reflux, 1 | 98 |
| 4 | **2a** | 3 | **3b** | 30, 24 | 96 |
| 5 | **2a** | 1 | **3b** | reflux, 1 | 92 |
| 6 | $Ph(CH_2)_2OH$ (**2b**) | 1 | **3a** | 30, 24 | 98 |
| 7 | **2b** | 5 | **3a** | 30, 5 | 93 |
| 8 | **2b** | 1 | **3a** | reflux, 0.5 | 98 |
| 9 | **2b** | 5 | **3b** | 30, 24 | 98 |
| 10 | **2b** | 1 | **3b** | reflux, 2 | 99 |
| 11 | **2b** | 1 | **3a** | reflux, 0.5[d] | 99 |
| 12 | **2b** | 1 | **3a** | reflux, 0.5[e] | 99 |
| 13 | **2a** | 5 | **3c** | 50, 15 | 98[f] |
| 14 | **2a** | 5 | **3d** | 50, 15 | 98 |
| 15 | **2a** | 5 | **3e** | 50, 15 | 97 |
| 16 | **2a** | 5 | **3f** | 50, 17 | 96 |
| 17 | $C_6H_{13}CH(OH)CH_3$ (**2c**) | 1 | **3a** | 30, 24 | 11 |
| 18 | **2c** | 10 | **3a** | reflux, 1 | 97 |
| 19 | $PhCH(OH)CH_3$ (**2d**) | 10 | **3a** | 30, 24 | 2 |
| 20 | **2d** | 10 | **3a** | reflux, 0.5 | 99 |
| 21 | cyclohexanol | 1 | **3a** | 30, 24 | 0 |
| 22 | $C_6H_5OH$ | 1 | **3a** | 30, 24 | 0 |
| 23 | geraniol | 1 | **3a** | 30, 22 | 98[g] |
| 24 | $TBSO(CH_2)_4OH$ | 1 | **3a** | 30, 23 | 98[h] |
| 25 | $THPO(CH_2)_4OH$ | 1 | **3a** | 30, 23 | 97[h] |
| 26 | $CF_3CO_2(CH_2)_4OH$ | 1 | **3a** | 30, 24 | 97[h] |
| 25 | $PhOC(O)C{\equiv}CH_2OH$ | 1 | **3a** | 30, 24 | 97 |

[a] Reaction conditions: **2** (5 mmol), **3** (3 mL). [b] Molarity on the basis of the monomeric formulation. [c] Isolated yield after column chromatography. [d] In **3a** (2.5 mL) and toluene (2.5 mL). [e] In **3a** (2.5 mL) and THF (2.5 mL). [f] Determined by $^1H$ NMR. [g] $Sc(OTf)_3$ gave a complex mixture. [h] $Sc(OTf)_3$ afforded $AcO(CH_2)_4OAc$ quantitatively.

The operation is quite simple (eq 1). A solution of alcohol **2** (5 mmol) and a catalytic amount of 1,3-dichlorotetrabutyldistannoxane (**1**)[15] in alkenyl ester **3** (3 mL) was stirred under conditions given in Table 1. The reaction mixture was




evaporated, and the residue was subjected to column chromatography to give the desired esters **4**. When the substrate is insoluble in the enol esters, a cosolvent like toluene or THF may be used. Notably, *enol esters and solvents can be used as received without purification and no inert atmosphere is necessary for the reaction* because of the stability of **1** under the ambient atmosphere. In the presence of 1 or 3 mol % of **1**, both **3a** and **3b** acetylated octanol quantitatively at 30 °C in 24 h (entries 1 and 4). The reaction time can be shortened by increasing the amount of the catalyst to 5 mol % (entries 2) or by elevating the reaction temperature (entries 3 and 5). 2-Phenylethanol reacted similarly (entries 6−10), and the use of cosolvent gave rise to virtually

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(14) For another transesterification under mild conditions: Imwinkelried, R.; Schiess, M.; Seebach, D. *Org. Synth.* **1987**, *65*, 230.

(15) Other distannoxanes such as isothiocyanato derivatives worked similarly.

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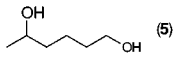
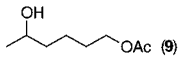
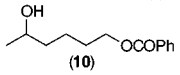
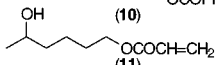
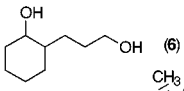
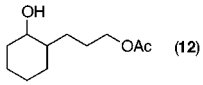
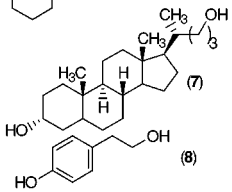
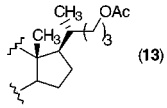
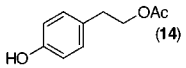
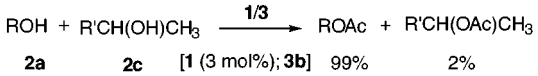
**Table 2. Selective Acylation of the Primary Hydroxyl in Diols and 2-Mercaptoethanol**

| entry | diol | reactn conditn | monoacetate (% yield) | %yield of diacetate |
|---|---|---|---|---|
| 1 |  (5) | **5** (3 mmol);**1** (2 mol%); **3b** (5 mL); 30 °C; 24 h |  (9) 92 | 1 |
| 2 | **5** | **5** (5 mmol);**1** (10 mol%); **3c** (3 mL); 50 °C; 40 h |  (10) 96 | 1 |
| 3 | **5** | **5** (5 mmol);**1** (10 mol%); **3d** (3 mL); 30 °C; 45 h |  (11) 96 | 0 |
| 4 | **5** | **5** (5mmol); $Sc(OTf)_3$ (1 mol%); $Ac_2O$ (3 mL); 30 °C, 24 h | 0 | 99 |
| 5 | **5** | **5** (5mmol)$Bu_3P$ (10 mol%); $Ac_2O$ (3 mL);0 °C, 24 h | 0 | 98 |
| 6 | **5** | **5** (5 mmol); DMAP (10 mol%); $Ac_2O$ (2 mL);pyridine (2 mL); | 0 | 88 |
| 7 |  (6) | 30 °C, 24 h **6** (3mmol);**1** (9 mol%); **3a** (2.7 mL); 30 °C; 24 h |  (12) 93 | 0 |
| 8 |  (7) | **7** (1mmol);**1** (2 mol%); **3a** (5 mL); THF (8 mL); 30 °C; 20 h |  (13) 84 | 4 |
| 9 |  (8) | **8** (5 mmol);**1** (5 mol%); **3a** (2.5 mL); THF (2.5 mL); 30 °C; 24 h |  (14) 99 | 0 |
| 10 | **8** | **8** (5 mmol);$Sc(OTf)_3$ (1 mol%); $Ac_2O$ (3 mL); 30 °C, 4 h | 0 | 91 |
| 11 | **8** | **8** (5 mmol); $Bu_3P$ (10 mol%); $Ac_2O$ (3 mL);30 °C, 4 h | 0 | 95 |
| 12 | **8** | **8** (5 mmol); DMAP (10 mol%); $Ac_2O$ (2 mL);pyridine (2 mL); 30 °C, 24 h | **14** 13 | 84 |

**Scheme 1**[a,b]



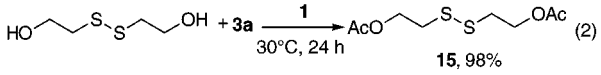

| | | | | |
|---|---|---|---|---|
| **2a** | **2c** | [**1** (3 mol%); **3b**] | 99% | 2% |
| **2b** | **2d** | [**1** (1 mol%); **3a**] | 99% | 1% |
| **2b** | **2d** | [**1** (1 mol%); **3b**] | 99% | 0% |

[a] Reaction conditions: alcohols, 5 mmol each, **3**, 5 mL; 30 °C. [b] Yields determined by GLC.

no influence (entries 11 and 12). Vinyl benzoate, acrylate, pivalate, and chloroacetate also afforded the desired esters quantitatively (entries 13−16). The reaction of secondary alcohols was controlled simply by changing the reaction temperature: the reaction was sluggish at 30 °C (entries 17 and 19) but proceeded quantitatively at refluxing temperature (72 °C) (entries 18 and 20). Cyclohexanol failed to react at 30 °C, and more remarkably, phenol did not undergo acetylation (entries 21 and 22). Acid-sensitive functional groups remained intact (entries 23−25). The trifluoroacetyl group, which is not tolerant of $Sc(OTf)_3$, survived (entry 26), and an acetylenic ester that decomposed upon exposure to $Bu_3P$ was employable (entry 27).

With these results in hand, we turned our attention to preferential acetylation of a primary alcohol over a secondary analogue.[16] As expected from the above results, competition reactions between these two types of alcohols at 30 °C resulted in selective or exclusive formation of primary acetates (Scheme 1). The unique selectivities are highlighted by intramolecular versions in Table 2, where results from some representative acidic and basic methods are also given for comparison. Only the distannoxane method exhibited the high preference for the primary hydroxyl over the secondary one (entries 1−3, 7, and 8), whereas the other methods afforded diacetates (entries 4−6). Marked discrimination was realized between phenol and primary hydroxyl (entry 9), while no such selectivity was attained by other methods (entries 10−12).

Another remarkable chemoselectivity is shown in eq 2. A disulfide linkage is completely tolerant in our procedure to give a quantitative yield of diacetate **15**, while the $Sc(OTf)_3$ and $Bu_3P$ methods resulted in the cleavage of the S−S bond to give $AcS(CH_2)_2OAc$ in 97 and 96% yields, respectively.




In summary, a new method for acylation of alcohols has been achieved. Its synthetic usefulness is apparent from the simple operation and high selectivities. The precedent efforts were directed mostly toward rendering the catalysts applicable to hindered alcohols,[2−6,11,12] and hence, the selective acylation has met with limited success.[16] In this respect, the distannoxane method is capable of complementing the existing methods. Of more practical importance is the stability of **1** toward hydrolysis and oxidation. Many acylation catalysts such as $Bu_3P$, $Sc(OTf)_3$, etc. need to be handled in an inert atmosphere. Moreover, because of its crystallinity and high melting point (107−110 °C), **1** has low toxicity and is readily separated from the reaction mixture by column chromatography or distillation of volatile esters. It is also to be noted that the catalyst **1** is prepared very easily by simply mixing $Bu_2SnO$ and $Bu_2SnCl_2$[17] or is even available from a commercial source.[18] As such, the distannoxane method will find a wide variety of synthetic uses.

**Supporting Information Available:** Experimental procedure and $^1H$ and $^{13}C$ NMR spectra of esters (2 pages).

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(16) For selective acylation of primary alcohols, see refs 8 and 9 and refereces cited therein.
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