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One-step conversion of silyl/THP ethers into the corresponding acetates

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Abstract—A variety of silyl and THP ethers were directly converted into the corresponding acetates using acetic anhydride in the presence of a catalytic amount of $Cu(OTf)_2$ in CH_2Cl_2 . It was observed that MEM ethers could also be cleaved under the same conditions. The reaction was also studied with other Lewis acids. © 2001 Elsevier Science Ltd. All rights reserved.

The acylation of alcohols is a useful transformation in day-to-day synthetic organic chemistry. Although there are several methods for conversion of alcohols into acetates under acidic and basic conditions,¹ methods for direct conversion of silyl/THP ethers into acetates are limited, and even those suffer from serious drawbacks. For example, the acetyl bromide/tin(II) bromide combination has been used for direct conversion of silyl ethers into acetates, but benzyl ethers are also cleaved under these conditions.² The FeCl₃/Ac₂O method also suffers from similar drawbacks where benzyl, methyl, and other ethers are also acylated.³ Similarly, conversion of tetrahydropyranyl (THP) ethers directly into acetates using AcOH/AcCl⁴ and TiCl₄/Ac₂O⁵ is known. These conditions are harsh and sensitive groups such as acetonides are also acylated under the reaction conditions. While working on the synthesis of (-)-carbovir,⁶ we observed that a *t*-butyldimethylsilyl (TBDMS) ether was directly converted into an acetate with Ac₂O in the presence of a catalytic amount of Cu(OTf)₂.⁷ We also observed that the method is mild and simple and that several silvl ethers were selectively acylated. The reaction was also extended to the conversion of THP ethers into acetates, and details are described in this paper.

At the outset, α -methylbenzyl alcohol was protected as the TBDMS ether and its conversion into an acetate (entry 1) was studied with Lewis acids such as Cu(OTf)₂, Sn(OTf)₂, ZnCl₂, BF₃·OEt₂, FeCl₃, and SnCl₄ in CH₂Cl₂ at room temperature (rt). It was observed that a catalytic amount (5 mol%) of Cu(OTf)₂ or Sn(OTf)₂ efficiently converted the TBDMS ether into the corresponding acetate in 2–3 h in 75 and 70% yield, respectively. Other Lewis acids were not satisfactory at all. For example, ZnCl₂ and BF₃·OEt₂, even in stoichiometric amounts, gave lower yields (56 and 12% yield, respectively) of the acetate. FeCl₃ and SnCl₄ did not give a clean reaction. The conversion of the above TBDMS ether into the acetate in the presence of Cu(OTf)₂ was also studied in several solvents such as CH₂Cl₂ (2.5 h, 75% yield), ether (24 h, 25% yield), MeCN (3 h, 51% yield), MeNO₂ (2.5 h, 64% yield), benzene (3.5 h, 40% yield). From these results, it was concluded that CH₂Cl₂ was the best solvent for this reaction. It was further observed that the trimethylsilyl (TMS) and tetrahydropyranyl (THP) ethers of α methylbenzyl alcohol could also be converted into acetates by using acetic anhydride in the presence of 5 mol% of Cu(OTf)₂ at room temperature (entries 2 and 3). In order to extend the scope of this reaction, a variety of silyl and THP ethers were prepared and used for their conversion into acetates (Table 1).

It was observed that methyl and benzyl ethers, which are cleaved with FeCl₃/Ac₂O,³ are unaffected under the present conditions (entries 12 and 21). The other interesting part of the reaction was that the acetonide group remained intact during the conversion of the TBDMS ether into an acetate group (entry 21). Allylic silyl ethers (entries 7 and 29) gave clean acetate products only when the reaction was carried out in the absence of solvent at lower temperature. It was observed that a primary TBDMS ether can be deprotected in preference to a secondary TBDMS ether with reasonable success (entry 24). The phenolic TBDMS ether remains unaffected under the above conditions (entry 25). It was also observed that a TBDMS ether can be converted into an acetate in the presence of a *t*-butyldiphenylsilyl

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Table 1. One-step conversion of silyl and THP ethers into acetates using Ac_2O in the presence of 5 mol % of $Cu(OTf)_2$

Entry	Substrate	Product	Temp.	Time (h)	Yield (%)
1.	OR R = TBDMS	OAc	rt	2.5	75
2.	R = TMS	\downarrow	rt	4.0	85
3.	Ph' Me R = THP	Ph' Me	rt	12	71
4.	PhCH ₂ OTBDMS	PhCH ₂ OAc	rt	2.5	63
5.	PhCH ₂ OTHP	2		12	80
6	OTBDMS	OAc	rt	3.0	68
0.		·"//Ph		5.0	00
7.	Ph	Ph	-25 - 0 °C	8.0	88
8.	\land R = TBDMS	$S \setminus \square$	rt	3.0	60
9.	\rangle Interior $R = TMS$		rt	3.0	79
10.	R = THP	Aco	rt	14	68
	RO OBz	QBz			
11.		OAc	rt	4.0	67
	Ph' V	OMe			
12.		,OAc	rt	3.0	65
	Ph OTBDMS	Ph OAc			
	\mathcal{A}	\sim			
13			rt	24	67
15.		Ţ ĨĒŢĒ	п	24	07
С		°~~~			
	OR	QAc			
14.			rt	8.0	68
15.	R = THP	l livie	rt	12	71
	\checkmark	\sim			
	OR	OAc			
16.	R = TBDMS	\wedge	rt	6.0	74
17.	R = TMS		rt	3.0	87
18.	R = THP	γ	rt	10	76
	t-BU OTBDMS	t-Bu OAc			
19.		\downarrow \sim \sim	rt	6.0	81
		Me Y			
	Me OTBDMS	Me OAc			
20.			rt	12	72
	OTBDMS	2 OAc			
		Me V			
21.	BnO	BnO	rt	6.0	81
22		Õ		10	67
22.	PhOCH ₂ CH ₂ OTBDMS PhOCH ₂ CH ₂ OTHP	PhOCH ₂ CH ₂ OAc	rt rt	12	67 67
25.	OTBDMS	OTBDMS OAc		12	07
24.	OTBDMS		MS _{rt}	3	70
	Ph Ph	83 % Ph 17 %		5	
	OTHP	OAc			
25.			rt	12	67
	TOTBDMS	TOTBDMS			
26.	CH ₃ (CH ₂) ₉ -OTHP	CH ₃ (CH ₂) ₉ -OAc	rt	10	91
	OTBDMS				
27.			rt	3	78
	OTBDMS	OTBDMS			
28.	TBDPSO-(CH ₂)8-OTBDMS	TBDPSO-(CH ₂) ₈ -OAc	rt	2	90
	\sim	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
29.	OTPOMS	OAc	-25 - 0 °C	8	
	/ ` OTBDPS	OTBDPS			
30.	.OTBDMS	,OAc	rt	5	89
	Ph OTROMO	Ph			
31			rt	8	92
51.	Ph	Ph	11	U	74
32	OMEM O	MEM OCH ₂ OAc	-25 - 0°C	3	77
54.	Ph OTBDMS Ph	OAc Ph OAc	20-0 C	5	11
		37 % 40 %			
33	CH ₃ (CH ₂) ₉ -OMEM CH ₃ (CH ₂) ₉	-OAc + CH ₃ (CH ₂) ₉ -OCH ₂ OAc	-25 - 0 °C	2	93
22 % 78 %					



Figure 1. Proposed catalytic cycle.

(TBDPS) ether (entries 28, 30 and 31). It was noticed from entries 32 and 33 that MEM ethers do not remain intact under this method.

Although we do not have any proof of the mechanism of this reaction, it is proposed that $Cu(OTf)_2$ reacts with Ac₂O to give AcOTf and Cu(OTf)OAc which then reacts with silyl, THP or MEM ethers to give the corresponding acetates whilst the catalyst is regenerated (Fig. 1). In conclusion, we have reported a very useful one-step transformation for conversion of silyl and THP ethers into acetates under very mild conditions.

General procedure: Acetic anhydride (1.2 mmol) was added dropwise to a solution of a substrate (1 mmol) in CH_2Cl_2 (5 mL) in the presence of 5 mol% of $Cu(OTf)_2$ at the temperature indicated in Table 1 and was stirred for an appropriate period of time (cf. Table 1). The reaction mixture was diluted with CH_2Cl_2 and washed with aqueous sodium bicarbonate solution and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated on a rotary evaporator. The crude product was purified over silica gel by column

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