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FACILE METHODS FOR THE DIRECT CONVERSIONS OF ARYL ACETATES INTO THE CORRESPONDING METHOXYMETHYL ETHERS OR SILYL ETHERS

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Abstract: Direct conversion of aryl acetates into aryl methoxymethyl ethers or aryl trialkylsilyl ethers was readily accomplished by treatment with methoxymethyl bromide or trialkylsilyl trifluoromethanesulfonate, respectively, in the presence of sodium methoxide.

Various types of protecting groups for the hydroxyl function have been extensively explored and are classified widely into four types, that is, alkyl ether-, silyl ether-, acetal-, and ester-types.[1] Direct transformation between four types of typical protecting groups of the hydroxylic function is of great importance from the standpoint of efficiency (time, reagents) and convenience, and we have reported several types of direct conversion of a protecting group of the hydroxylic function into another.[2]

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In a previous paper,[3] we have demonstrated that an ester-type protecting group of phenols can be efficiently converted into benzyl-protected phenols in good yields under the influence of a combination of benzyl bromide and sodium methoxide (Scheme 1). This suggested that the usage of a methoxymethylating agent or trialkylsilylating agent in place of benzyl bromide would afford directly the acetal-type or silyl ether-type protected phenols.

In this communication we report highly convenient methods for the direct conversion of aryl acetate into aryl methoxymethyl (MOM) ethers or aryl silyl ethers in a *one-pot* procedure.

First, we examined the reaction of aryl acetate with methoxymethyl chloride (MOMCl) instead of benzyl bromide under the same reaction conditions;[3] however, the desired aryl MOM ether was obtained in poor yield. After screening the reaction conditions, we found that short exposure of aryl acetate with sodium methoxide (30 min) before addition of the methoxymethylating agent gave a better result and that MOMBr was more effective than MOMCl. We chose tentatively the optimum reaction conditions as follows. To a solution of sodium methoxide (1.4 equiv.) in DMF was added aryl acetate at room temperature. After stirring for 30 min, 2 equiv. of MOMBr was added and stirred for 10 min. Using this procedure, various aryl acetates were converted into the corresponding MOM ethers in good yields (Table 1). As shown in Run 6, the carbonyl function was tolerated under these conditions, although the yield of MOM ether slightly decreased. When benzyloxymethyl (BOM) chloride was used instead of MOMBr, the corresponding BOM ethers were also obtained in good yields (Runs 2 and 8).

Scheme 1

$$\mathrm{ArOAc} + \overset{\text{1.2 equiv.}}{\mathrm{BnBr}} \xrightarrow[\text{DMF / r t / 0.5 h}]{\substack{\text{1.4 equiv.}\\ \text{NaOMe}}} \underset{\text{81 - 100\%}}{\mathrm{ArOBn}}$$

Table 1. Synthesis of Various Aryl MOM Ethers from Aryl Acetates [a]

$$\mathrm{ArOAc} \xrightarrow[\text{DMF / r t / 30 min}]{\text{NaOMe}} \xrightarrow[\text{10 min}]{\text{RX}} \mathrm{ArOR}$$

Run	ArOAc	RX	Yield [b] / %
1	4-BrC_6H_4OAc	MOMBr [c]	85
2	4-BrC_6H_4OAc	BOMCl [d]	92
3	2-BrC_6H_4OAc	MOMBr	87
4	3,4-$Me_2C_6H_3OAc$	MOMBr	82
5	4-$MeOC_6H_4OAc$	MOMBr	94
6	4-AcC_6H_4OAc	MOMBr	74
7	2-$C_{10}H_7OAc$ [e]	MOMBr	82
8	4-MeC_6H_4OAc	BOMCl	94

a) Molar ratio of ArOAc : NaOMe : RX = 1 : 1.4 : 2

b) Isolated yield of purified product.

c) MOM = CH_3OCH_2 d) BOM = $PhCH_2OCH_2$

e) 2-$C_{10}H_7$ = 2-naphthyl

Table 2. Synthesis of Various Aryl Silyl Ethers from Aryl Acetates [a)]

$$\mathrm{ArOAc} \xrightarrow[\mathrm{DMF\,/\,r\,t\,/\,0.5\ h}]{\mathrm{NaOMe}} \xrightarrow[\mathrm{1\ h}]{\mathrm{R_3SiOTf}} \mathrm{ArOSiR_3}$$

Run	ArOAc	R_3SiOTf	Yield [b)] / %
1	$2\text{-}MeC_6H_4OAc$	TBSOTf [c)]	93
2 [d)]	$3\text{-}MeC_6H_4OAc$	TBSOTf	85
3	$4\text{-}MeC_6H_4OAc$	TBSOTf	93
4	$4\text{-}MeC_6H_4OAc$	TESOTf [e)]	93
5	$3,4\text{-}Me_2C_6H_3OAc$	TBSOTf	93
6	$4\text{-}BrC_6H_4OAc$	TBSOTf	83
7	$4\text{-}MeOC_6H_4OAc$	TBSOTf	92
8	$4\text{-}MeOC_6H_4OAc$	TESOTf	88
9	$4\text{-}AcC_6H_4OAc$	TBSOTf	62
10 [f)]	$2\text{-}AcOC_6H_4OAc$	TBSOTf	89

a) Molar ratio of ArOAc : NaOMe : R_3SiOTf = 1 : 1.4 : 3

b) Isolated yield of purified product. c) TBS = $t\text{-}BuMe_2Si$

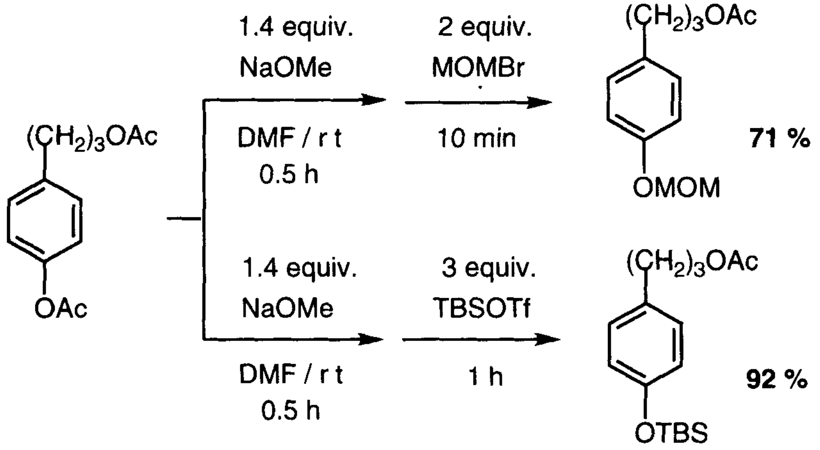
d) 1.2 equiv. of NaOMe was used. e) TES = Et_3Si

f) 2.8 equiv. of NaOMe and 6 equiv. of TBSOTf were used.

Next, we examined the direct conversion of aryl acetates into aryl silyl ethers. In the case of this direct conversion, a short reaction time (30 min) before addition of the silylating agent gave also a better result. As shown in Table 2, the acetyl protecting group for the phenolic hydroxyl function was removed readily to afford the corresponding silyl-protected phenols by the use of *t*-butyldimethylsilyl triflate (TBSOTf) or triethylsilyl triflate (TESOTf) in the presence of a stoichiometric amount of sodium methoxide.[4] As expected, the yield of the corresponding silyl ethers was improved by increasing the amount of trialkylsilyl triflate. And bis-acetate of catechol was successfully transformed into bis-TBS ether (Table 2, Run 10).

On the other hand, aliphatic acetates were unchanged under similar reaction conditions. So we tried chemoselective transformation between aryl acetate and aliphatic acetate, and the satisfactory results are shown in Scheme 2.

Scheme 2



In our series of studies on the one-step conversion between typical protecting groups of the hydroxyl function, we have added new direct conversion of the ester-type protecting group into the acetal-type one or the silyl ether-type one.

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References and Notes

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4. Typical experimental procedure for the direct conversion of an ester-type protecting group into a silyl ether-type one is as follows: to a solution of sodium methoxide (28.7 mg, 0.531 mmol) in DMF (1 ml) was added 1-acetoxy-4-methylbenzene (57.6 mg, 0.384 mmol) in DMF (1.5 ml) under argon atmosphere. After stirring for 0.5 h at room temperature, *t*-butyldimethylsilyl triflate (0.264 ml, 1.15 mmol) in DMF (1 ml) was added and stirring was continued for 1 h at room temperature. The mixture was then quenched with a phosphate buffer (pH 7). The organic materials were

extracted with Et_2O and the combined extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by thin-layer chromatography on silica gel to give 1-*t*-butyldimethylsilyloxy-4-methylbenzene (79.6 mg, 93%).

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