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HF–Pyridine: A Versatile Promoter for Monoacylation/Sulfonylation of Phenolic Diols and for Direct Conversion of *t*-Butyldimethylsilyl Ethers to the Corresponding Acetates

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Monoacylation and trifluoromethanesulfonylation of phenolic diols were achieved by the aid of HF–pyridine, whereas diacylation occurred with pyridine alone. Furthermore, HF–pyridine was found to promote the direct conversion of *t*-butyldimethylsilyl ethers to the corresponding acetates.

Monoprotection of diols is an important problem in organic synthesis,[1] and several methods to achieve this have been reported to date. For example, Babler and Coghlan reported monoacetylation of symmetric diols using an AcOH–H_2SO_4–H_2O system.[2] Nishiguchi and Taya reported selective monoacylation of 1,*n*-diols catalyzed by metallic sulfates supported on silica gel.[3] Nishiguchi's group also reported monoacylation of 1,*n*-diols catalyzed by ion-exchange resins.[4] More recently, monoacylation of multi-hydroxy groups of a carbohydrate was accomplished using an elegantly designed acylation catalyst developed by Kawabata.[5]

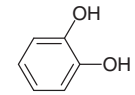
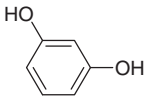
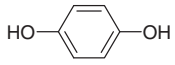
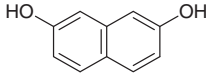
With respect to operational simplicity, direct conversion of one protective group into another protective group is desirable.[6] Oriyama revealed a variety of one-step conversions of one protective group to another group, such as the direct conversion of *p*-methoxybenzyl ethers into silyl ethers.[7]

Herein, we will describe HF–pyridine-promoted monoprotection of phenolic diols, which is in contrast to the pyridine-promoted reaction, and direct conversion of *t*-butyldimethylsilyl ethers into the corresponding acetates by the aid of HF–pyridine.

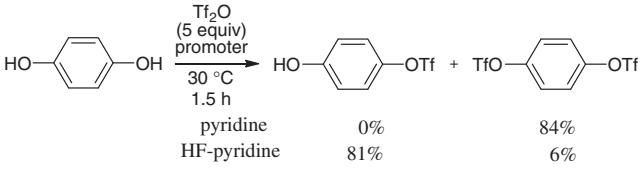
During the course of our study of HF–pyridine-promoted aryl *C*-glycosidation of glycals,[8] we found that HF–pyridine also promoted the acetylation of phenolic hydroxy groups. Therefore, we turned our attention to the monoacetylation of phenolic diols. We first examined the reactions of catechol (**1**), resorcinol (**2**), hydroquinone (**3**), and 2,7-naphthalenediol (**4**) with 5 equiv of acetic anhydride (Ac_2O) in the presence of pyridine or 70% HF–pyridine (Table 1). In all cases examined, when using pyridine as a promoter, only diacetates were obtained in high yields (96–98%). When HF–pyridine was used as the promoter, monoacetates were predominantly obtained. There was little difference in reactivity among the substitution patterns of the hydroxy groups (ortho, meta, and para) (Entries 2, 4, and 6).[9] We confirmed HF–pyridine retarded both the first and the second acetylation step. It should be mentioned that the separation of the monoacetates and diacetates was easily carried out by silica gel column chromatography using a mixture of hexane and ethyl acetate (3:1) as an eluent.

In the trifluoromethanesulfonylation of hydroquinone (**3**), similar phenomena were observed as shown in Scheme 1. The reaction of hydroquinone (**3**) with Tf_2O (Tf: $-SO_2CF_3$) promoted by pyridine gave only the ditriflate, whereas the reaction in the presence of HF–pyridine afforded predominantly the monotriflate. In the absence of promoter, the yields of monotriflate, ditriflate, and recovery of starting material were 23%, 0%, and 62%, respectively.

Table 1. Monoacetylation of phenolic diols[a]

Entry	Substrate	Promoter	Conditions		Yield[b]/%	
			Temp/°C	Time/h	Mono-acetate	Di-acetate
1	 **1**	pyridine	0	0.5	0	96
2		HF–pyridine	27	1.5	70	12
3	 **2**	pyridine	0	0.5	0	97
4		HF–pyridine	20	1.0	63	16
5	 **3**	pyridine	0	0.5	0	98
6		HF–pyridine	20	1.5	74	13
7	 **4**	pyridine	0	0.5	0	96
8		HF–pyridine	27	2.0	64	28

[a]All reactions were carried out using 5 equiv of Ac_2O in the presence of 1.5 equiv of pyridine (Entries 1, 3, 5, and 7) or 15 equiv of HF–pyridine (Entries 2, 4, 6, and 8). CH_2Cl_2 was used as a solvent in the case of pyridine. [b]Isolated yield by silica gel column chromatography using a mixture of hexane and ethyl acetate (3:1).

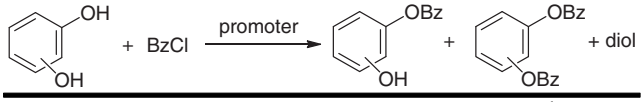


Scheme 1. Monotrifluoromethanesulfonylation of **3**.

For benzoylation instead of acetylation, the tendency of pyridine and HF–pyridine was also the same. In the case of pyridine, dibenzoate was produced predominantly (but not exclusively), whereas HF–pyridine gave the monobenzoate selectively. Little difference was observed between BzCl and Bz_2O as benzoylating reagents (Table 2).

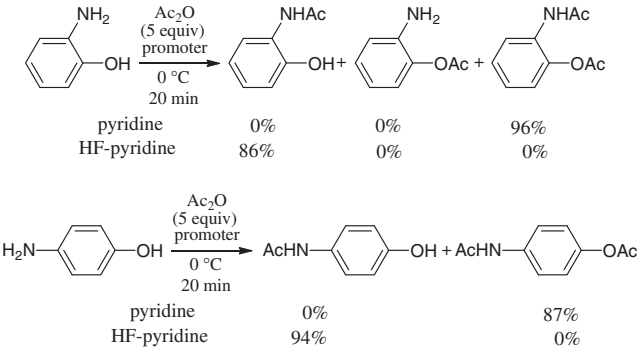
In the acetylation of 2- and 4-aminophenol (Scheme 2),[10] only the diacetate was obtained in the presence of pyridine, whereas only *N*-acetylated product was obtained in the presence of HF–pyridine.

Table 2. Benzoylation of catechol (**1**), resorcinol (**2**), and hydroquinone (**3**)[a]



Entry	Substrate	Promoter	Conditions		Yield[b]/%	
			Temp /°C	Time /h	Mono-benzoate	Di-benzoate
1	**1**	pyridine	25	15	18	71
2	**1**	HF–pyridine	25	15	71	22
3[c]	**1**	pyridine	26	24	16	75
4[c]	**1**	HF–pyridine	26	24	68	22
5	**2**	pyridine	28	2	16	60
6	**2**	HF–pyridine	28	2	60	16
7	**3**	pyridine	30	1	18	65
8	**3**	HF–pyridine	30	1	64	20

[a]All reactions were carried out using 5 equiv of BzCl in the presence of 1.5 equiv of pyridine (Entries 1, 3, 5, and 7) or 15 equiv of HF–pyridine (Entries 2, 4, and 8). [b]Isolated yield. [c]Bz_2O (5 equiv) was used.



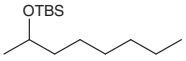
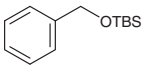
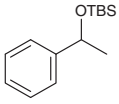
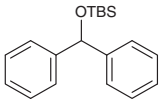
Scheme 2. Monoacetylation of 2- and 4-aminophenol.

Unfortunately, monoacetylation of aliphatic diols was unsuccessful. In all cases examined such as *trans*- and *cis*-1,2-cyclohexanediol and 1,8-octanediol using either pyridine or HF–pyridine as promoters, monoacetylated products were obtained predominantly with only moderate selectivities.

In 1974, Ganem and Small reported an $FeCl_3$–Ac_2O system for the direct conversion of *t*-butyldimethylsilyl ethers to acetates.[11] Danishefsky and Mantlo used this method for the synthesis of (±)-heptelidic acid.[12] Kim and Lee reported the reaction of silyl ethers with acid chlorides in the presence of zinc chloride to give the corresponding carboxylic esters including acetates.[13] Oriyama reported that a stoichiometric amount of acyl bromide and a catalytic amount of tin(II) promoted the conversion of silyl ethers into acetates.[14,15] We examined the reactions of several *t*-butyldimethylsilyl ethers with HF–pyridine as shown in Table 3. In all cases examined, the corresponding acetates were obtained in high yields.

In summary, we have discovered the HF–pyridine-promoted monoacylation of phenolic diols and direct conversion of *t*-butyldimethylsilyl ethers to the corresponding acetates.[16,17]

Table 3. HF–pyridine-promoted direct conversion of *t*-butyldimethylsilyl ethers to the corresponding acetate

Entry	Substrate[a]	HF–pyridine[b]	Conditions		Yield[c]/%
			Temp/°C	Time/h	
1		5.0	19	5	88
2		4.5	20	2.5	97
3		4.7	19	3	91
4		4.8	19	2.5	92

[a]TBS: *t*-butyldimethylsilyl. [b](mL of HF–pyridine)/(g of substrate). [c]Isolated yield.

References and Notes

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9 When one equiv of Ac_2O was used for **1**, **2**, and **3**, monoacetylated products were predominantly obtained approximately equally in both case of pyridine and HF–pyridine (monoacetate:diacetate = 63:13 for **1**).
10 In the reactions promoted by pyridine described in Schemes 1 and 2, CH_2Cl_2 was used as a solvent.
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16 Experimental procedure for acetylation using HF–pyridine: To a polyethylene vessel containing phenolic diol, HF–pyridine (15 equiv) was added, followed by addition of Ac_2O (5 equiv). After stirring at the indicated temperature for the indicated amount of time, the mixture was poured into a solution of saturated aqueous KF solution. The mixture was extracted by ethyl acetate, then the organic layer was washed with 1 M HCl, saturated $NaHCO_3$, and brine. After evaporation, the residue was purified by silica gel column chromatography to give the monoacetylated and diacetylated products.
17 Experimental procedure for *t*-butyldimethylsilyl ethers to acetates using HF–pyridine: In a polyethylene vessel was placed the *t*-butyldimethylsilyl ether. The amount was described in Table 3. Addition of Ac_2O (5 equiv) followed by confirmation of completion of the reaction, the usual workup was performed as described above to give the corresponding acetate.

