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Bu_4NF-Acid Combination as a Novel Class of Mild and Selective Deprotecting Reagents for Enol Ethers

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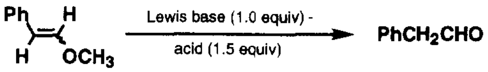
Abstract: Bu_4NF-acid combined reagents selectively deprotect enol ethers,such as 1-methoxy-1,3-dienes and β-alkoxystyrenes, leading to the corresponding aldehydes with good to quantitative yields.

Conversion of enol ethers to aldehydes is carried out generally in the presence of strong mineral acids such as aqueous HCl, H_2SO_4, and $HClO_4$.[2] If another acid sentitive group exists in the molecule containing an enol ether, the treatment with strong acids may either remove such an acid-labile group or decompose substrate completely. We have recently reported $Bu_4NF\text{-}BF_3{\cdot}OEt_2$ combination as a new selective reagent for facile conversion of γ-alkoxyallylstannanes to 3-stannylpropanal.[3] In order to clarify whether the $Bu_4NF\text{-}BF_3{\cdot}OEt_2$ is only effective combination among various Lewis base-acid complexes, and whether the combination is effective only for γ-alkoxyallylstannanes or it is more general in character and may be applied to the deprotection of wide range of organic enol ethers, we have examined deprotection of several enol ethers, which are unstable and easily polymerized under ordinary acidic conditions, by using different Lewis base-acid combined reagents. We now report that Bu_4NF-acid combined reagents are quite effective for deprotecting acid-labile enol ethers and act as a so-called *"(Lewis) acid buffer"* system.



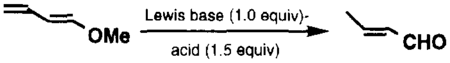
1 2

Table 1 . Deprotection of β-methoxystyrene **1**[a]

LB^c \ A^b	$BF_3{\cdot}Et_2O$	$BF_3{\cdot}2H_2O$	$AlCl_3{\cdot}Et_2O$	$ZrCl_4$	$HfCl_4$	HCl^d
none	e	e	e	e	e	62[f]
Bu_4NF	88	72	52	82	41	47
THF	e	34	e	e	e	65
Ph_3N	e	e	e	e	e	80
Ph_3P	52	54	38	8	35	58
Ph_3As	e	e	e	24	24	73
Ph_3Sb	e	e	e	e	e	55

[a] Procedure: **1**(0.1mmol) was added at 0°C to a stirred mixuture of Lewis base, acid and H_2O(1.0:1.5:2.0) in CH_2Cl_2(1ml). Reactions were carried out until total disappearance of **1**(by TLC). Then, the mixture was quenched with aqueous $NaHCO_3$(sat) and filtered through silica-gel. [b] A=acid. [c] LB=Lewis base. [d] 1.0M HCl(dry) in Et_2O. [e] total decomposition. [f] yield of **2**(%) was determined by capillary GLC using dodecane as an internal standard. All experiments were run at least three times and average data are presented in the table.

First, we tested various Lewis base-acid combinations as a potential reagent for deprotection of β-methoxystyrene **1**[4]. The results are summarized in Table 1. PPh_3 and Bu_4NF appeared to be the most effective among Lewis bases tested. The combination of Bu_4NF with almost all Lewis acids listed in Table 1 provided aldehyde **2** with good to excellent yields which were comparable to the yield obtained using HCl itself, and in the case of $BF_3{\cdot}Et_2O$ (88%) and $ZrCl_4$(82%) the yields were even better than those for HCl. In contrast with deprotection using HCl alone[2c-f], the use of single Lewis acids or combination of those Lewis acids with Ph_3N and Ph_3Sb lead to total decomposition of **1**. Use of tetrahydrofuran and triphenylarsine in combination with Lewis acids is not effective for deprotection of **1**; decomposition of **1** took place or **2** was obtained in low yields. Best combinations for deprotection of **1**:(Bu_4NF-A and Ph_3P-A) were applied for deprotection of acid-sensitive 1-methoxy-1,3-butadiene **3** and the data are summarized in Table 2. Bu_4NF-acid combination was effective for selective deprotection of extremely acid-sensitive substrate **3**; E-crotonaldehyde **4** was obtained in modest to good yield.[5] Attempts to deprotect **3** by use of uncomplexed acids as well as by combination of those acids with Ph_3P failed. In addition Bu_4NF-$BF_3{\cdot}Et_2O$ and $Bu_4NF{\cdot}HCl$ combined reagents were effective for deprotection of 1-methoxy-cyclohexa-1,3-diene **5**; the ketone **6** was obtained in 57% and 95% yield, respectively. Use of $BF_3{\cdot}Et_2O$ completely decomposed **5** and use of HCl lead to isomeric ketones containing **6** with total 20% yield.

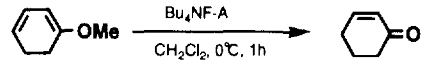


3 **4**

Table2. Deprotection of 1-methoxy-1,3-butadiene **3**[a]

LB \ A	$BF_3{\cdot}Et_2O$	$BF_3{\cdot}2H_2O$	$AlCl_3{\cdot}Et_2O$	$ZrCl_4$	$HfCl_4$	HCl
none	b	b	b	b	b	b
Bu_4NF	81[c]	79	65	26	18	81
Ph_3P	trace	trace	b	trace	b	b

[a] Procedure is similar to that for deprotection of **1**. [b] Total decomposition. [c] Yield of **4** was determined by ^1H NMR analysis.



5 **6**

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4 To avoid misunderstanding it should be pointed out that **I** has no another acid labile group in the molecule and may be easily deprotected by use of a simple Brønsted acid such as HCl, and the transformation from **1** to **2** was chosen only as a convenient model to know how effective the acids or combination reagents are for deprotection of enol ethers.

5 E-Crotonaldehyde **4** obviously is thermodynamically controlled product, which is obtained presumably *via* isomerization of less stable 3-butenal.

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