Zinc Tetrafluoroborate-Catalyzed Efficient Conversion of Aldehydes to Geminal Diacetates and Cyanoacetates

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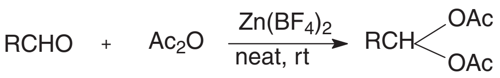
A trace of an aqueous solution of zinc tetrafluoroborate was demonstrated to catalyze the conversion of an aldehyde to its 1,1-diacetate by acetic anhydride without any solvent. A similar reaction of an aldehyde with a mixture of potassium cyanide and acetic anhydride in methylene chloride was also catalyzed by $Zn(BF_4)_2$ to provide the corresponding geminal cyanoacetate.

The protection of an aldehyde is a useful process and often required in a multistep synthetic strategy. As an alternative to acetals[1] the geminal diacetates are gaining much importance in organic synthesis as aldehyde protecting groups because of their stability in neutral and basic media.[2] Moreover, the diacetates of α, β-unsaturated aldehydes serve as important building blocks for the synthesis of dienes to be used for Diels-Alder reactions.[3] Usually, diacetates are prepared from the reaction of aldehydes and acetic anhydride under the catalysis of a variety of protic or Lewis acids. These include strong acids like sulfuric acid,[4a] phosphoric acid,[4b] perchloric acid[4c] and methanesulfonic acid[4d] and Lewis acids such as $ZnCl_2$,[5a] $FeCl_3$,[5b] PCl_3,[5c] $Sc(OTf)_3$,[5d] $Cu(OTf)_2$,[5e] $Bi(OTf)_3$,[5f] $LiBF_4$,[5g] NBS,[5h] and I_2.[5i] Some solid acid catalysts, e.g. Nafion-H[6a] and zeolites,[6b,6c] are also used. However, many of these procedures are associated with disadvantages like long reaction time, low yield of products, use of expensive and toxic catalysts. Hence, a practical and more efficient alternative using an inexpensive and environment friendly reagent is still of interest.

Fluoroboric acid (HBF_4) and its salt, particularly lithium tetrafluoroborate ($LiBF_4$) have been used widely as Lewis catalysts in a variety of reactions.[7] However, HBF_4 is a strong acid and $LiBF_4$ is very expensive and moisture sensitive. On the other hand, an aqueous solution of zinc tetrafluoroborate is readily available and very cheap. Thus, we have envisioned the use of $Zn(BF_4)_2$ as a convenient and practical alternative Lewis catalyst and as a part of this program we have already demonstrated its successful application in the deprotection of *tert*-butyldimethylsilyl ether[8a] and Mannich-type reaction of aldimines with silyl enol ethers.[8b] We would like to disclose here that a trace of an aqueous solution of $Zn(BF_4)_2$ efficiently catalyzes the formation of 1,1-diacetate by a reaction of an aldehyde and acetic anhydride without any solvent (Table 1). We have also observed that aldehydes react with acetic anhydride and potassium cyanide in methylene chloride under the catalysis of $Zn(BF_4)_2$ to provide the corresponding 1,1-cyanoacetate (Table 2).

In a typical experimental procedure, a mixture of aldehyde (1 mmol) and acetic anhydride (freshly distilled, 1 mmol) was stirred at room temperature in the presence of a catalytic amount of an aqueous solution (40 wt.%) of zinc tetrafluoroborate (0.6 mol% with respect to aldehyde) for a certain period of time as required to complete the reaction (TLC). The reaction mixture was quenched with a few drops of water and extracted with ether. The ether extract after being washed with aqueous $NaHCO_3$ and brine was dried (Na_2SO_4) and evaporated to give the crude product. Although this material was found to be reasonably pure further purification was done by distillation under reduced pressure or by column chromatography over silica gel. Gram scale (1–2 g) reactions were also carried out without any difficulty following the same procedure.

Table 1. The $Zn(BF_4)_2$ catalyzed conversion of aldehydes to 1,1-diacetates



Entry	Aldehyde	Time/h	Yield/%[a]
1	PhCHO	3	95
2	4-(OMe)-C_6H_4CHO	4	95
3	4-(Cl)-C_6H_4CHO	2	94
4	4-(NO_2)-C_6H_4CHO	3[b]	93
5	Piperonal	2.5	94
6	3-(O-allyl)C_6H_4CHO	2	93
7	3-(O-CH_2CO_2Et)C_6H_4CHO	2	86
8	3-(O-Bz)C_6H_4CHO	3	90
9	3-(O-PNB)C_6H_4CHO	3	88
10	Furfural	1.5	85
11	Thiophene-2-carboxaldehyde	2.5	92
12	Cinnamaldehyde	1.5	95
13	Acrolein	1.5[c]	71
14	Crotonaldehyde	1.5[c]	84
15	$C_9H_{19}CHO$	3[c]	65
16	C_3H_7CHO	3[c]	70
17	$(CH_3)_2CHCHO$	3[c]	60

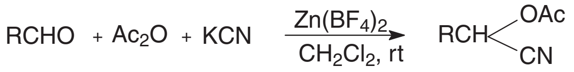
[a] Yields refer to pure isolated products characterized by spectral data (IR, ^1H, ^{13}C NMR). [b] The reaction was carried out at 50 °C. [c] The reaction was carried out at 5-10 °C.

Several structurally varied aldehydes underwent acetylations by this procedure to provide the corresponding 1,1-diacetates in excellent yields. The results are reported in Table 1. The present procedure is effective for aromatic, heteroaromatic, open-chain conjugated and saturated aldehydes although the yields for aliphatic saturated aldehydes (entries 15–17) are relatively low, being associated with the formation of some of the vinyl acetate. The presence of electron-donating and electron-withdrawing groups on the aromatic ring of aldehydes does not make any difference in the acetylation. The reaction conditions are mild enough not to induce any isomerization for conjugated aldehydes (entry 14) and any damage to moieties like O-Me (entry 2), *O*-allyl (entry 6), CO_2Et (entry 7), *O*-benzyl (entry 8), *O-p*-nitrobenzyl (entry 8) which often undergo cleavage under strong acidic reaction medium. A few acid sensitive aldehydes such as piperonal (entry 5), furfural (entry 10) and thiophene aldehyde (entry 11) are also diacetylated by this procedure without any difficulty. Most significantly, the conversion under the catalysis of $Zn(BF_4)_2$ are relatively fast (1.5–4 h) compared to the procedure using more expensive $LiBF_4$ (16–25 h).[5g]

In a similar procedure, when the aldehyde was stirred with a mixture of acetic anhydride and potassium cyanide in methylene chloride in the presence of an aqueous solution of $Zn(BF_4)_2$ (0.6 mol%) at room temperature for 3–20 h the corresponding cyanoacetate was obtained in good yield. The results are presented in Table 2. It has been observed that for an efficient reaction a large excess (10–13 equiv.) of KCN is required[9] and without any solvent the reaction became exothermic and vigorous. Methylene chloride has been found to be the solvent of choice. In general, all the reactions are very clean and high yielding. However, it has been observed that ketones remained inert under the present procedure, making it selective for aldehydes.

In conclusion, this zinc tetrafluoroborate-catalyzed procedure provides a highly efficient methodology for the conversion of aldehydes to the corresponding 1,1-diacetates and cyanoacetates. The significant advantages of this procedure are: a) operational simplicity, b) considerably fast reaction, c) high yields, d) mild reaction condition compatible with sensitive molecules, e) truly catalytic, and f) cost efficiency. We believe, this will offer a better and more practical alternative to the existing procedures.[4–6] Further expansion of the use of this catalyst for other useful reactions are in progress.

Table 2. The $Zn(BF_4)_2$ catalyzed conversion of aldehydes to 1,1-cyanoacetates



$$RCHO + Ac_2O + KCN \xrightarrow[CH_2Cl_2,\ rt]{Zn(BF_4)_2} RCH\begin{cases} OAc \\ CN \end{cases}$$

Entry	Aldehyde	Time/h	Yield/%[a]
1	PhCHO	5	98
2	4-(Cl)-C_6H_4CHO	5	98
3	Piperonal	8	92
4	4-(OMe)-C_6H_4CHO	9	83
5	Furfural	5	87
6	Thiophene-2-carboxaldehyde	20	78
7	3-(O-allyl)-C_6H_4CHO	8	90
8	Cinnamaldehyde	3	80
9	$C_9H_{19}CHO$	6	63
10	Crotonaldehyde	3	62
11	Citral	3	54

[a] Yields refer to pure isolated products characterized by spectral data (IR, ^1H, ^{13}C NMR).

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