LiBF₄-Mediated Conversion of Aldehydes to gem-Diacetates

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Abstract: An efficient and highly selective method for the conversion of aldehydes to *gem*-diacetates is described using lithium tetrafluoroborate under mild reaction conditions. Due to the neutral reaction conditions, this method is compatible with acid-sensitive protecting groups such as acetonides, carbamates, THP and TB-DMS ethers present in the substrate.

Key words: lithium tetrafluoroborate, aldehydes, gem-diacetates

The protection of aldehydes as gem-diacetates plays an important role in organic synthesis because they are useful precursors¹ for synthetically useful acetoxy dienes and dihalo vinyl acetates. In addition, acylals are useful as crosslinking reagents² for cellulose in cotton and serve as activators³ in the composition of the bleaching mixture used for the treatment of wine-stained fabrics. Furthermore, gem-diacetates are useful intermediates for nucleophilic substitution reactions.⁴ Due to the remarkable stability of gem-diacetates toward a variety of reaction conditions, they are gaining importance in organic synthesis as an alternative to acetals for the protection of aldehydes. Generally, gem-diacetates are prepared from aldehydes and acetic anhydride using strong Brønsted acids⁵ or Lewis acids as catalysts.⁶ Recently, metal triflates, iodine and NBS have also been employed for this transformation.⁷ However, many of these methods employ strongly acidic or oxidizing conditions, expensive and hazardous reagents and cumbersome experimental/ product isolation procedures. Furthermore, very few methods are known for the chemoselective acetalization of aldehydes in the presence of ketones. However, the development of a neutral alternative would extend the scope of this transformation. Recently, lithium tetrafluoroborate in acetonitrile (LTAN) has emerged as a powerful reaction medium for effecting various transformations including the hydrolysis of acetals, desilylation of ethers, Diels-Alder reactions and glycosidation reactions.⁸

In line with the recent surge in activity in the use of $LiBF_4$ as a mild Lewis acid, we report herein a simple and efficient procedure for the conversion of aldehydes into *gem*-diacetates using lithium tetrafluoroborate under neutral conditions.⁹ The treatment of benzaldehyde with acetic anhydride in the presence of lithium tetrafluoroborate in acetonitrile at ambient temperature resulted in the formation of benzal diacetate in 90% yield. In a similar fashion,

various substituted aldehydes reacted well with acetic anhydride to give the corresponding acylals in high yields (Scheme).

 $\begin{array}{c} O \\ R \\ H \\ H \\ 1 \\ 2 \\ \end{array} + (Ac)_2 O \\ CH_3 CN, r.t. \\ RCH(OAc)_2 \\ 3 \\ Scheme \\ \end{array}$

The reactions proceeded smoothly at ambient temperature and the products were obtained in excellent yields with high chemoselectivity. Ketones such as cyclohexanone, acetophenone and 3-pentanone did not yield any acylals under the present reaction conditions. Furthermore, the chemoselectivity of the present method was exemplified by the use of ketoaldehyde (entry h). This indicates that chemoselective protection of an aldehyde in the presence of ketone could be achieved by this procedure. However, the reactions did not proceed in the absence of lithium tetrafluoroborate. Both aromatic and aliphatic aldehydes gave the corresponding acylals in high yields (80–93%) in a short reaction time (3.5–7.5 h). However, aromatic aldehydes with electron withdrawing groups like 4-nitrobenzaldehyde required comparatively longer reaction time to achieve complete conversion. The products were obtained in pure form after aqueous work-up without further purification. Acid-sensitive substrates like furfural and cinnamaldehyde are also protected as gem-diacetates in high yields without the formation of any side products, which are normally observed under strongly acidic conditions. The tolerance of various functional groups under the present reaction conditions have been examined by reacting the substrates bearing OPh, OMe, methylenedioxy, nitro, and olefinic groups. The major advantage of this procedure is in the selective protection of aldehydes as gem-diacetates in the presence of highly acid sensitive acetals, cabamates, TBDMS and THP ethers, which do not survive under strongly acidic conditions. Due to mild reaction conditions employed for this transformation, a number of functional groups, which are capable of reacting with LiBF₄ remain intact. There are several advantages in the use of LiBF₄ for this transformation, which avoids the use of strongly acidic or basic conditions. Thus, this method is mild and tolerates a wide range of functional groups. Best results were obtained with an equimolar ratio of LiBF₄, acetic anhydride, and aldehyde. Several examples illustrating this novel and rapid procedure for the preparation of *gem*-diacetates are summarized in the

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Table. The *gem*-diacetates can be conveniently deprotected to their parent aldehydes using aqueous potassium carbonate under mild conditions.^{6a}

Entry	Substrate	Product	Reaction Time (h)	Yield ^b (%)
a	СНО	3a	4.5	90
b	MeO CHO	3b	4.0	92
c	CHO	3c	5.0	93
d	ζ_L _{CHO}	3d	4.0	89
e	ССНО	3e	3.5	87
f	СНО	3f	4.5	90
g	ССНО	3g	5.0	88
h	ССНО	3h	4.5	87
i	PhOCHO	3i	5.0	90
j	O,N CHO	3ј	7.5	80
k	СНО	3k	5.0	85
1	СНО	31	4.0	83
m		3m	4.5	85
n	СНО	3n	5.5	90
0	— сно	30	5.0	85
р	ВпО	3p	4.0	90
q	тнро	3q	5.0	85
r	TRDMSO	3r	4.5	80

TableLiBF4-Mediated Conversion of Aldehydes to gem-Diace-
tates^a

^a All products were characterised by IR, ¹H NMR, mass spectral data and also comparison with authentic samples.

^b Isolated yields after recrystallization (ethyl acetate-hexane, 2:8).

In summary this paper describes a mild and efficient method for the conversion of aldehydes to *gem*-diacetates using LiBF_4 under neutral conditions thereby leaving acid and base-labile protecting groups intact. The high levels of chemoselectivity in this process combined with a simple operation, high yields and cleaner reaction profiles will find a wider use of the diacetate-protecting group in organic synthesis.

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- (9) Preparation of gem-Diacetates: A mixture of aldehyde (5 mmol) freshly distilled acetic anhydride (5 mmol) and LiBF₄ (5 mmol) in acetonitrile (15 mL) was stirred at r.t. for an appropriate time (Table). After complete conversion, as indicated by TLC, the reaction mixture was poured into sat. sodium bicarbonate solution (30 mL) and extracted with ethyl acetate (2×15 mL). The combined organic layers were dried over anhyd Na₂SO₄ and concentrated in vacuo. The resulting product was recrystallized from ethyl acetatehexane (2:8) to afford pure 1,1-diacetate. Spectral data. **3b**: Solid, mp 72–74 °C, ¹H NMR (CDCl₂): δ = 2.18 (s, 6 H), 3.88 (s, 3 H), 3.89 (s, 3 H), 6.83 (d, 1 H, J = 8.0 Hz), 7.03 (s, 1 H), 7.08 (d, 1 H, J = 8.0 Hz), 7.58 (s, 1 H). MS (EI): *m*/*z* = 268 [M⁺], 167, 139, 95, 77, 43. IR (KBr): 3049, 2955, 1745, 1687, 1495, 1243, 1010, 968 cm⁻¹. 3d: Solid, mp 66–67 °C (ref.⁶ 66–67). ¹H NMR $(CDCl_3)$: $\delta = 2.15$ (s, 6 H), 7.10 (dd, 1 H, J = 5.0, 4.5 Hz), 7.30 (d, 1 H, J = 4.5 Hz), 7.40 (d, 1 H, J = 5.0 Hz), 7.90 (s, 1 H). MS (EI): m/z = 214 [M⁺], 171, 155, 112, 85. IR(neat): 3050, 2960, 1757, 1480, 1245, 1017, 845 cm⁻¹. **3f**: Solid, mp 84–85 °C (ref.⁵ 84–86). ¹H NMR (CDCl₃): δ = 2.15 (s, 6 H), 5.95 (dd, 1 H, J = 16.5 and 7.2 Hz), 6.85 (d, 1 H, J = 16.5

Hz), 7.20–7.45 (m, 6 H). MS (EI): m/z = 234 [M⁺], 191, 175, 132, 101, 91. IR (KBr): 3055, 2955, 1750, 1680, 1490, 1240, 1015, 970 cm⁻¹. **3h**: ¹H NMR (CDCl₃): $\delta = 2.20$ (s, 6 H), 7.80 (t, 2 H, J = 8.2 Hz), 7.60 (s, 1 H), 7.65 (m, 1 H), 7.95 (d, 2 H, J = 8.2 Hz). MS (EI): m/z = 236 [M⁺], 193, 105, 77, 51, 43. IR (KBr): 3055, 2970, 1760, 1720, 1235, 1020 cm⁻¹. **3i**: ¹H NMR (CDCl₃): $\delta = 2.16$ (s, 6 H), 6.98–7.05 (m, 3 H), 7.08–7.20 (m, 3 H), 7.30–7.38 (m, 3 H), 7.60 (s, 1 H). MS