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An Improved Method for the Synthesis of Allylic *gem*-Diacetates from α,β-Unsaturated Aldehydes Catalyzed by Lithium Tetrafluoroborate

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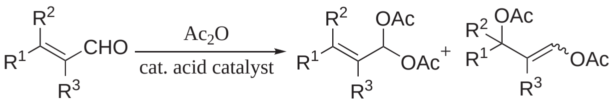
An improved method for the synthesis of allylic *gem*-diacetates (acylals) is described. The desired acylals are obtained by the reaction of α,β-unsaturated aldehydes with acetic anhydride using a catalytic amount of lithium tetrafluoroborate in diethyl ether at room temperature.

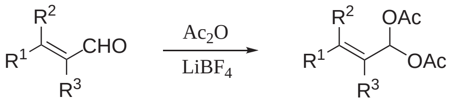
Allylic *gem*-diacetates (acylals) have demonstrated a wide range of applicability in directing organometallic transformations.[1] The allylic diacetates are generally prepared by reaction of α,β-unsaturated aldehydes and acetic anhydride catalyzed by a variety of acid catalysts. However, significant amounts of rearranged products (vinyl acetates) are also produced under these conditions (Scheme 1). Although Trost et al. recently reported that iron(III) chloride was the best catalyst for this reaction among the various acid catalysts they tested,[1h,1l] this involves some annoying problems. (1) Because iron(III) chloride catalyzes not only the acylal formation but also its rearrangement, it is necessary to quench the reaction before the complete consumption of the starting aldehyde in order to obtain the desired product with highly isomeric purity. (2) Aldehydes with a tertiary alkyl ether functional group, which is readily cleaved by iron(III) chloride, cannot be used. Thus, development of more efficient catalysts for this reaction is still actively pursued by synthetic chemists. As part of our ongoing program in developing new synthetic methods using lithium salts as mild Lewis acid catalysts,[2] we wish to report our findings wherein lithium tetrafluoroborate has been identified as a mild and effective acid catalyst for this transformation.

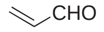
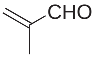
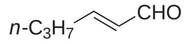
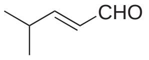
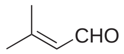
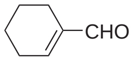
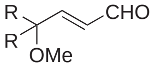
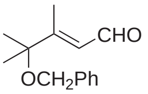
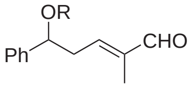
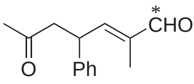
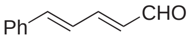
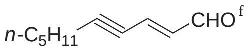
Initially, (E)-2-hexenal was treated with 2.0 equiv of acetic anhydride in the presence of 10 mol % of $LiBF_4$ in diethyl ether at room temperature for 2 h. After completion of the reaction (monitored by GLC), the usual work-up of the reaction mixture afforded crude product. GLC analysis of the crude product showed the formation of (E)-2-hexene-1,1-diyl diacetate and 1-hexene-1,3-diyl diacetate in 93.4% and 1.5% yields, respectively. Short column chromatography on silica gel provided isomerically pure (E)-2-hexene-1,1-diyl diacetate in 88% yield (Table 1, Entry 3).[3] Because of the low acidity of $LiBF_4$, rearrangement was almost completely suppressed and the acylal formation mainly proceeded. A screening of solvents revealed that diethyl ether as a solvent gave the best result.[4] Iron(III) chloride protocol gave the product in 67% yield and with 96% isomeric purity after silica gel flash chromatography.[1h]



Scheme 1.

Table 1. Preparation of allylic *gem*-diacetates from α,β-unsaturated aldehydes using $LiBF_4$[a]



Entry	Substrate	Time /h	Yield /%[b]
1[c]		22	83
2[c]		22	87
3		2	88[d]
4		1.5	91[d]
5		2	100
6		4	78[d]
			
7[c]	R = R = n-C_3H_7	5	76
8[c]	R–R = $(CH_2)_5$	4	78
9[c]		8	79
			
10[c]	R = Ac	6.5	89
11[c]	R = CH_2OMe	0.25	80
12[c]	R = $SiMe_2$-t-C_4H_9	8.5	89
13[c]		12	80
14		23	90
15[c]		4	79[f]

[a]Conditions: substrate (2.0 mmol), Ac_2O (4.0 mmol), $LiBF_4$ (0.20 mmol), Et_2O (2 mL), rt (15–25 °C), unless otherwise noted. [b]Isolated yield of isomerically pure product. [c]$LiBF_4$ (0.60 mmol) was used. [d]Trace amount of vinyl acetate (1.5–3.5% checked by GLC) was detected in the crude product. [e]Asterisk signifies the reactive site. [f]$E/Z = 90/10$.

The scope and generality of the present method was then tested by converting various other α,β-unsaturated aldehydes into the corresponding *gem*-diacetates and the results are summarized in Table 1. A wide range of mono-, di-, and trisubstituted substrates underwent smooth diacetylation without any trace of by-products arising from rearrangement (Entries 1, 2 and 5, and 7–15). The case of (*E*)-4-methyl-2-pentenal (Entry 4) and 1-cyclohexene-1-carboxaldehyde (Entry 6) is worth mentioning as these gave the desired acylals in 91% and 78% yields by our method, in contrast to relatively moderate yields (64% and 50%) of products by the $FeCl_3$ protocol.[11] Notably, aldehydes with a tertiary alkyl ether functional group, which undergoes acylal formation by the Trost method with difficulty,[11] could easily be converted into the corresponding *gem*-diacetates in good yields (Entries 7–9).[5] A variety of functional groups such as benzyloxy (Entry 9), acetoxy (Entry 10), methoxymethoxy (Entry 11), *tert*-butyldimethylsiloxy (Entry 12), and ketone (Entry 13) remained intact under our reaction conditions. Exposure of α,γ-dienal (Entry 14) and α,γ-enynal (Entry 15) to $LiBF_4/Ac_2O$ furnished the corresponding *gem*-diacetates in 90% and 79% yields, respectively. These results clearly indicate the mildness and the versatility of the present protocol.[6]

In conclusion, we have developed a mild and efficient method by which allylic *gem*-diacetates can be prepared from α,β-unsaturated aldehydes and acetic anhydride in the presence of catalytic of lithium tetrafluoroborate in good to high yields.

References and Notes

1 For example, see: a) A. Ghribi, A. Alexakis, J. F. Normant, *Tetrahedron Lett.* **1984**, *25*, 3079. b) X. Lu, Y. Huang, *J. Organomet. Chem.* **1984**, *268*, 185. c) B. M. Trost, J. Vercauteren, *Tetrahedron Lett.* **1985**, *26*, 131. d) B. M. Trost, C. B. Lee, J. M. Weiss, *J. Am. Chem. Soc.* **1995**, *117*, 7247. e) C. W. Holzapfel, L. Marais, *Tetrahedron Lett.* **1998**, *39*, 2179. f) F. R. van Heerden, J. J. Huyser, D. Bradley, G. Williams, C. W. Holzapfel, *Tetrahedron Lett.* **1998**, *39*, 5281. g) J. S. Yadav, B. V. S. Reddy, G. S. K. K. Reddy, *Tetrahedron Lett.* **2000**, *41*, 2695. h) B. M. Trost, C. B. Lee, *J. Am. Chem. Soc.* **2001**, *123*, 3671. i) B. M. Trost, C. B. Lee, *J. Am. Chem. Soc.* **2001**, *123*, 3687. j) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921. k) M. B. Deshmukh, S. D. Jadhav, A. R. Mali, A. W. Suryawanshi, P. V. Anbhule, S. S. Jagtap, S. A. Deshmukh, *Synth. Commun.* **2005**, *35*, 2967. l) B. M. Trost, M. L. Crawley, C. B. Lee, *Chem.—Eur. J.* **2006**, *12*, 2171. m) M. S. Reddy, M. Narender, Y. V. D. Nageswar, K. R. Rao, *Synth. Commun.* **2007**, *37*, 1983.

2 a) F. Ono, R. Negoro, T. Sato, *Synlett* **2001**, 1581. b) Y. Nakae, I. Kusaki, T. Sato, *Synlett* **2001**, 1584. c) N. Sumida, K. Nishioka, T. Sato, *Synlett* **2001**, 1921. d) N. Hamada, K. Kazahaya, H. Shimizu, T. Sato, *Synlett* **2004**, 1074. e) K. Kazahaya, S. Tsuji, T. Sato, *Synlett* **2004**, 1640. f) N. Hamada, T. Sato, *Synlett* **2004**, 1802.

3 $LiBF_4$ was the best catalyst among the lithium salts examined under identical conditions: LiBr (0%), $LiNTf_2$ (0%), LiOTf (0%), and $LiClO_4$ (0%).

4 Hexane (80%), THF (0%), EtOAc (0%), and CH_3CN (0%).

5 When iron(III) chloride was used as catalyst in the reaction of (2*E*)-4-methoxy-4-propyl-2-heptenal (neat, rt), a complex mixture was obtained as indicated by TLC, and the desired acylal was isolated in 35% yield.

6 Typical procedure (Table 1, Entry 3): A mixture of (*E*)-2-hexenal (197 mg, 2.0 mmol), Ac_2O (409 mg, 4.0 mmol), $LiBF_4$ (18.8 mg, 0.20 mmol), and Et_2O (2 mL) was stirred at room temperature for 2 h (monitored by GLC). After the reaction was quenched with sat. $NaHCO_3$ (2 mL), the resulting mixture was extracted with EtOAc (20 mL × 2). The combined extracts were successively washed with sat. $NaHCO_3$ (10 mL) and with sat. NaCl (10 mL). The organic layer was dried (Na_2SO_4) and concentrated. GLC analysis of the crude product indicated the formation of (*E*)-2-hexene-1,1-diyl diacetate and 1-hexene-1,3-diyl diacetate in 93.4% and 1.5% yields relative to n-$C_{15}H_{32}$ as an internal standard. The crude product was purified by short column chromatography on silica gel (3% EtOAc–hexane) affording isomerically pure (checked by GLC and 500 MHz ^1H NMR) (*E*)-2-hexene-1,1-diyl diacetate (353 mg, 88%).

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