# Gallium(III) chloride: an efficient catalyst for facile preparation of *gem*-diacetates from aldehydes

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**Abstract**
An efficient, facile preparation of *gem*-diacetates or diacetoxy acetals from aldehydes in excellent yields, catalyzed by $GaCl_3$, under solvent-free conditions, is described herein.

**Keywords:** Gallium(III) chloride, aldehydes, *gem*-diacetates, acetic anhydride, solvent- free

## Introduction

Selective protection of carbonyl function as *gem*-diacetates (acylals) or *gem*-bis(acyloxy)-alkanes is an important transformation in organic chemistry[1] as an alternative to acetals because of their stability under neutral and basic conditions[1b] as well as under critically controlled acidic conditions. Apart from mere protective groups acylals are important synthons and are useful precursors. The acylals derived from α-β unsaturated aldehydes are important starting materials for Diels-Alder reactions.[2] These *gem*-diacetates have several synthetic as well as industrial applications. In industries, diactetates are utilized as cross linking reagents[3] in cellulose and cotton industry, being also used as stain bleaching agents. As synthons, acylals have been exploited in well known reactions of organic chemistry, like Grignard,[4] Barbier,[4b] and Prins[5] reactions, condensation reactions of Knoevenagel,[6a] and benzoin[6b] type, and are also used in the synthesis of chrysanthemic acid,[7a] and the total syntheses of sphingofungins E and F.[7b] Because of their synthetic and industrial utility and unique properties as protective groups as well as important synthons, a search for efficient and facile preparation of acylals is of current interest. Apart from other methods, conventionally *gem*-diacetates are prepared from aldehyde, acetic anhydride and a catalyst *viz* strong Bronsted acids[8] like $H_2SO_4$, $H_3PO_4$, and super acids[9] like Nafion-H and heteropolyacids. The use of strong Lewis acids[10] like $BF_3$, $PCl_3$, $ZnCl_2$, $LiBF_4$, $ZrCl_4$, $Er(OTf)_3$, $FeCl_3$, $FeCl_3/SiO_2$, $Zn(ClO_4)_2.6H_2O$, *etc* have also been reported. In addition to these catalysts, graphite, zeolites, tungstosilicic acid and zirconium sulfophenyl phosphonate have also been employed in this protection process.[11] Some of these methods still suffer from drawbacks like prolonged reaction time (*viz*. up to 120 h in case of 2-furyl aldehyde with $PCl_3$),

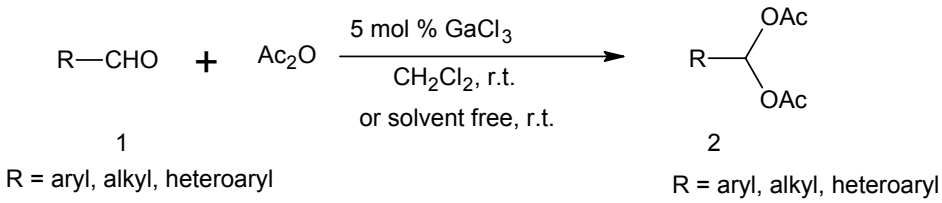
 

low yields in the cases of 4-nitrobenzaldehyde (4 %) and cinnamaldehyde (30 %), when $PCl_3$, is used and, in some cases, requirement of elevated temperature. Moreover, several of these catalysts are unsafe to handle, like metal perchlorates, $BF_3$, etc. Consequently it seems desirable and necessary to develop a simple, safe, efficient and facile method for the preparation of these *gem*-diacetates.

Though indium and gallium both are in same group i.e. IIIA, indium and its salts have been studied extensively and the results of this prolific exploration are reviewed from time to time,[12] while gallium and its salts remained almost ignored. Yet, the comparable ionization potentials ( Ga: FIP, 5.99 eV, $E^o$, $Ga^{+3}$/Ga = - 0.56 V; In: FIP, 5.79 eV, $E^o$, $In^{+3}$/In = -0.345 V ) indicate they should have equally attractive properties. Very recently, the use of gallium is reported in some major reactions of organic chemistry like Reformatsky,[13] Barbier,[14] Grignard,[15] bromination of aromatics[16a] and allylation of indoles.[16b] The applications of gallium(III) halides are developing[17] at a very fast pace, showing that its utility can match indium.[18]

## Results and Discussion

In continuation of our own work[19] on the use of gallium and its salts, in this communication we wish to report a gallium(III) chloride catalyzed preparation of *gem*-diacetates, from aldehyde and acetic anhydride (Scheme 1).




**Scheme 1**

In initial experiments, we used varying quantities of catalyst, *viz.* from 1 mol% to 20 mol% (Table1). Indeed, we were able to establish the optimum quantity of the catalyst at 5 mol%. In a pilot experiment, *p*-tolualdehyde, acetic anhydride, and $GaCl_3$ (1:1.5:0.05), in dichloromethane (Method A), were stirred at room temperature for 3 min to obtain *gem*-diacetate in 98 % yield.

To show the wide application of this procedure, other aldehydes were reacted analogously to afford *gem*-diacetates in 80-98 % yields. Under these conditions, reaction time was reduced dramatically and reaction completes within 3-14 minutes (Method A, Table 2). After this success we looked for further improvements in this process, *viz*. to carry this reaction under solvent-free conditions, at room temperature. (Method B). Under solvent-free conditions, equivalent results were obtained and reaction times shortened to 1-6 minutes, affording *gem*-diacetates in 82-98 % yields.

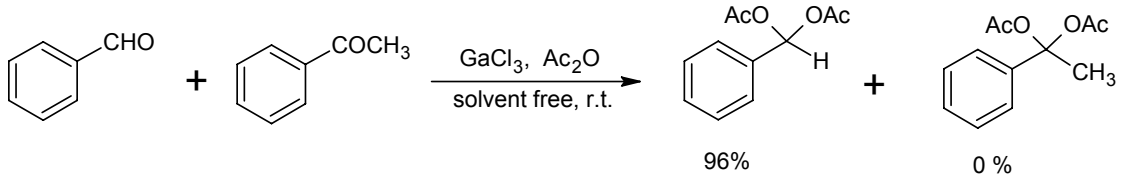
 

**Table 1.** **S**ynthesis of aldehyde *gem*-diacetates using varying amount of catalyst

| S. No. | Amount of $GaCl_3$ (mol%) | Yield[a] (%) Method A[b] | Method B[c] |
|---|---|---|---|
| 1 | 1 | 85 | 86 |
| 2 | 2 | 89 | 92 |
| 3 | 5 | 97 | 98 |
| 4 | 10 | 97 | 97 |
| 5 | 20 | 98 | 97 |

[a]Yields refers to pure isolated product, [b] Aldehyde (2 mmol), acetic anhydride (3 mmol), $CH_2Cl_2$, room temperature, [c] Aldehyde (2 mmol), acetic anhydride (3 mmol), solvent-free, room temperature

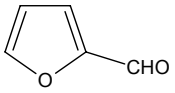
A variety of aromatic, aliphatic and heterocyclic aldehydes are converted to corresponding *gem*-diacetates using acetic anhydride in the presence of $GaCl_3$, in excellent yields, at room temperature, and in very short reaction times. All aromatic aldehydes carrying electron-donating or electron-withdrawing substituents reacted well, however, as one can see from Table 2, yields are slightly lower in aromatic aldehydes with electron-withdrawing groups and in case of conjugated aldehydes, particularly for crotonaldehyde and acrolein (entry 10-11, Table 2). This decrease in the yields may be due to the formation of polymeric materials as side products, which is to be expected. To show the selectivity/chemoselectivity of the reaction, it was performed using a mixture of aldehydes and ketones, from which only aldehyde diacetates were obtained (Scheme 2), the ketones remaining unaffected, as illustrated by acetophenone and benzophenone (entries 13-14, Table 2).




**Scheme 2**

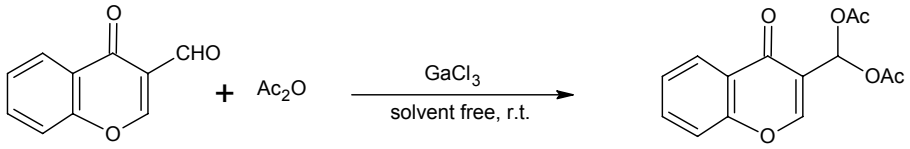
Furthermore, when aldehyde and ketone groups are present in the same molecule, only the aldehyde diacetate was obtained, the ketone moiety remaining intact (Scheme 3). When this reaction was extended to 3-formyl benzopyran-(4*H*)-4-one, its formyl diacetate was obtained in excellent yields (Scheme 3).

**Table 2.** $GaCl_3$ catalysed synthesis of aldehyde *gem*-diacetates

| Entry | Substrates | Product[a] | Time (min) | | Yield[b] (%) | |
|---|---|---|---|---|---|---|
| | | | Method A | Method B | Method A | Method B |
| 1 | PhCHO | **2a** | 3 | 1 | 96 | 98 |
| 2 | 4-Me-$C_6H_4CHO$ | **2b** | 3 | 1 | 97 | 98 |
| 3 | 4-MeO-$C_6H_4CHO$ | **2c** | 4 | 2 | 94 | 95 |
| 4 | 4-Cl-$C_6H_4CHO$ | **2d** | 4 | 2 | 93 | 97 |
| 5 | 3-$NO_2$-$C_6H_4CHO$ | **2e** | 14 | 5 | 91 | 89 |
| 6 | 4-$NO_2$- $C_6H_4CHO$ | **2f** | 14 | 6 | 89 | 91 |
| 7 | PhCH=CHCHO | **2g** | 8 | 4 | 87 | 86 |
| 8 | $CH_3(CH_2)_2CHO$ | **2h** | 7 | 3 | 90 | 90 |
| 9 | $CH_3(CH_2)_4CHO$ | **2i** | 5 | 3 | 86 | 91 |
| 10 | $CH_3CH$=CHCHO | **2j** | 5 | 4 | 86 | 89 |
| 11 | $H_2C$=CHCHO | **2k** | 5 | 2 | 80 | 83 |
| 12 |  | **2l** | 4 | 2 | 83 | 82 |
| 13 | $PhCOCH_3$ | — | 6[e] | 6[e] | - | — |
| 14 | PhCOPh | — | 6[e] | 6[e] | - | — |

Method A: Aldehyde (2 mmol), acetic anhydride (3 mmol), $GaCl_3$ (5 mol %) in $CH_2Cl_2$ stirred at room temperature; Method B: Aldehyde (2 mmol), acetic anhydride (3 mmol), $GaCl_3$ (5 mol %) in solvent-free condition stirred at room temperature

[a] All the products were characterized by comparison of their spectral and physical data with those of authentic samples. [b] Isolated yields of corresponding *gem*-diacetates. [e] Time in hours.




**3** **4**

92% ($CH_2Cl_2$, r.t., 12 min), 94% (solvent-free, r.t., 3 min)

**Scheme 3**

## Conclusions

In conclusion, the present method is a very simple, mild, efficient and convenient catalytic method for the preparation of *gem*-diacetates from aldehydes under solvent-free conditions using

$GaCl_3$. In addition, this protocol has advantages in term of short reaction times, high yields, high selectivity, fairly wide scope and avoidance of rigorous reaction conditions.

## Experimental Section

**General Procedures.** IR spectra were obtained with a Perkin-Elmer 237B infra red spectrometer, from KBr pellets. $^1$H NMR spectra were recorded in FT-NMR-AL300 spectrometer using tetramenthylsilane (TMS) as internal standard. $GaCl_3$ used was commercial grade and was not further purified. Acetic anhydride was distilled prior to use.

**General procedure for the preparation of *gem*-diacetates – Method A**

To a stirred solution of aldehyde (2 mmol) and acetic anhydride (3 mmol) in dichloromethane (10 mL), $GaCl_3$ (17.5 mg, 5 mol%) was added, and the mixture was stirred at room temperature for the time indicated in Table 2. After reaction completion, the reaction mixture was diluted with dichloromethane and washed with saturated $NaHCO_3$ solution (3 x 15 mL), and then with saturated brine. The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated in *vacuo* to afford the pure corresponding *gem*-diacetates.

**General procedure for the preparation of *gem*-diacetates under solvent-free conditions – Method B**

To a stirred solution of aldehyde (2 mmol) in acetic anhydride (3 mmol), $GaCl_3$ (17.5 mg, 5 mol %) was added, and the mixture was stirred at room temperature for the time indicated in Table 2. After completion of reaction, the reaction mixture was extracted with dichloromethane and washed with saturated $NaHCO_3$ solution (3 x 15 mL), and then with saturated brine. The organic layer was dried over anhydrous $Na_2SO_4$ and concentrated in *vacuo* to afford the pure corresponding *gem*-diacetates.

**Representative spectral data**

**2b.** M.p. 81-82 $^o$C, Lit[9] M.p. 81-82; IR (KBr): 2950, 1771, 1742, 1510, 1398, 1250, 1010, 960 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.66 (s, 1H), 7.38 (d, $J$ = 8.2 Hz, 2H), 7.21 (d, $J$ = 8.2 Hz, 2H), 2.40 (s, 3H), 2.14 (s, 6H); Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.86; H, 6.30. Found: C, 64.96; H, 6.21.

**2f.** M.p. 124-125 $^o$C, Lit[9] M.p. 124-125; IR (KBr): 2952, 1760, 1619, 1525, 1351, 1239, 1200, 995 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.30 (d, $J$ = 7.9 Hz, 2H), 7.70 (d, $J$ = 7.9 Hz, 2H), 7.52 (s, 1H), 2.15 (s, 6H); Anal. Calcd for $C_{11}H_{11}NO_6$: C, 52.17; H, 4.34; N, 5.53. Found: C, 52.10; H, 4.25; N, 5.45.

**2g.** M.p. 83-85 $^o$C, Lit[9] M.p. 84-86; IR (KBr): 2945, 1758, 1604, 1501, 1402, 1249, 1198, 1009, 940 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.29-7.38 (m, 6H), 7.01 (d, 1H), 6.20-6.72 (m, 1H), 2.11 (s, 6H); Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.67; H, 5.98. Found: C, 66.90; H, 6.17.

**2j.** liquid; IR (KBr): 2950, 1755, 1398, 1246, 1216 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.80 (d, $J$ = 6.1 Hz, 1H), 5.20-6.10(m, 2H), 1.86-2.11 (m, 9H); Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 6.97. Found: C, 55.99; H, 6.79.
**4.** M.p. 131-132$^oC$; IR (KBr) 3085, 2987, 2940, 1761, 1645, 1625, 1612, 1470, 1417, 1245, 1192, 1073, 933$cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ =8.27 (d, $J$ = 9.0 Hz 1H), 8.24 (s, 1H),7.71 (m, 1H, ArH), 7.61 (s, 1H), 7.48-7.52 (m, 2H, ArH), 2.16 (s, 6H); Anal. Calcd for $C_{14}H_{12}O_6$ C, 61.32; H 3.68. Found: C, 6139; H, 3.59.

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