Copper(II) Tetrafluoroborate-Catalyzed Formation of Aldehyde-1,1-di-acetates

Asit K. Chakraborti,* Ramasamy Thilagavathi, Raj Kumar
National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S. A. S. Nagar, Punjab – 160062, India
Fax +91(172)2214692; E-mail: akchakraborti@niper.ac.in
Received 21 January 2004; revised 4 February 2004
Dedicated to Prof. Harkishan Singh.

Abstract: Aldehyde 1,1-diacetates are formed in excellent yields from aldehydes and acetic anhydride under solvent-free conditions at room temperature in short times in the presence of a catalytic amount of copper(II) tetrafluoroborate hydrate.

Keywords: 1,1-diacetates, copper compounds, catalysis, solvent-free reactions

The formation of 1,1-diacetates (acylals) constitutes a valuable method for the protection of aldehydes because acylals are generally stable under neutral, acidic, and basic media adopted for routine work-up procedures.¹⁻³ In addition to serve as a masked aldehyde function, the 1,1-diacetates find numerous applications. The ambident nature of 1,1-diacetates,⁴ makes them synthetically important precursors of 1-acycloxydienes⁵ and 2,2-dichlorovinyl acetate⁶ for Diels–Alder reactions. Compounds bearing the 1,1-diacetate functionality are used as cross-linking agents for cellulose in cotton⁷ and activators in the composition of bleaching mixtures for wine-stained fabrics.⁸ Classically, acylal formation involves the reaction of aldehydes with Ac₂O in the presence of strong protic acids.⁹ Various organic¹⁰ and inorganic Lewis-acid catalysts that include metal halides,¹¹ solid acids,¹² metal tetrafluoroborates,¹³ and metal triflates¹⁴ have been introduced. The existing methodologies of acylal formation suffer from disadvantages such as prolonged reaction times, high temperatures, use of solvents, use of moisture sensitive and costly catalysts, special efforts being required to prepare the catalyst (e.g., Nafion-H, FeCl₃–SiO₂), need to use excess Ac₂O, and requirement of special apparatus. Thus, there was a necessity to develop a better catalyst for 1,1-diacetate formation.

Recently, we reported that metal tetrafluoroborates activate anhydrides for the acylation of alcohols, phenols, thiols, and amines.¹⁵ We disclose herein our findings on the catalytic effects of Cu(BF₄)₂·xH₂O for 1,1-diacetate formation from aldehydes.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R¹ = R² = H</td>
<td>2</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>R¹ = H</td>
<td>2</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>R¹ = H</td>
<td>2</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>R¹ = H</td>
<td>2</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td>R¹ = H</td>
<td>2</td>
<td>95</td>
</tr>
<tr>
<td>6</td>
<td>R¹ = H</td>
<td>2</td>
<td>88</td>
</tr>
<tr>
<td>7</td>
<td>R¹ = CF₃</td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>R¹ = H</td>
<td>3</td>
<td>92</td>
</tr>
<tr>
<td>9</td>
<td>R¹ = NO₂</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>10</td>
<td>R¹ = H</td>
<td>2</td>
<td>94</td>
</tr>
<tr>
<td>11</td>
<td>R¹ = CHO</td>
<td>3</td>
<td>93</td>
</tr>
<tr>
<td>12</td>
<td>R¹ = H</td>
<td>2</td>
<td>90</td>
</tr>
<tr>
<td>13</td>
<td>R¹ = CHO</td>
<td>20</td>
<td>97</td>
</tr>
<tr>
<td>14</td>
<td>R¹ = OMe</td>
<td>20</td>
<td>94</td>
</tr>
</tbody>
</table>

SYNTHESIS 2004, No. 6, pp 0831–0833
Advanced online publication: 05.03.2004
© Georg Thieme Verlag Stuttgart · New York
Diverse aldehydes were subjected to 1,1-diacetate formation by the treatment with Ac$_2$O under the catalytic influence of Cu(BF$_4$)$_2$·xH$_2$O (Table 1). Optimum conditions for the reaction are 1.5 equivalents of Ac$_2$O in the absence of solvent at room temperature. The use of 1 equivalent of Ac$_2$O afforded comparable results, however, required relatively longer reaction times and in some cases the reaction did not proceed to completion as the solid product, which formed trapped the starting aldehydes. The rate of the reaction was found to be very fast and in most of the cases the diacetate formation was completed in 1–20 minutes (TLC, IR, NMR) with excellent yields. The progress of the reaction can be monitored visually. For aromatic aldehydes, a clear solution is obtained after the addition of Ac$_2$O, and the formation of a solid (except for entries 1, 3, and 7) indicates completion of the reaction. For aliphatic aldehydes, the reaction becomes exothermic after the addition of Ac$_2$O, indicating the completion of diacetate formation. In general, the products obtained after work-up were clean (spectral analyses) and did not require any further purification. The reaction works well for aromatic and aliphatic aldehydes. However, no diacetate formation was observed for acetophenone (entry 21). The reaction rate was found to be dependent on the steric crowding surrounding the aldehyde group. Thus, the presence of the OMe group in 2-methoxy-1-naphthaldehyde (entry 13) necessitates the use of excess of Ac$_2$O and longer reaction time. The two peri hydrogens in 9-anthraldehyde (entry 14) offer steric inhibition for the diacetate formation resulting in an increase in the reaction time.

In conclusion, Cu(BF$_4$)$_2$·xH$_2$O is a novel and highly efficient catalyst for 1,1-diacetate formation from aldehydes. The advantages are high yields, fast reaction, low cost of the catalyst, and operation at room temperature. With the increasing tight legislation on the release of waste and use of toxic substances as a measure to control environmental pollution, the solvent-free conditions employed in the present method make it "environmentally friendly".

### Table 1 Cu(BF$_4$)$_2$·xH$_2$O Catalyzed 1,1-Diacetate Formation of Different Aldehydes with Ac$_2$O (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time (min)</th>
<th>Yield (%)$^{a,b,c}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>R = Ph</td>
<td>10</td>
<td>96$^a$</td>
</tr>
<tr>
<td>16</td>
<td>R = Me</td>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>17</td>
<td>R = H</td>
<td>1</td>
<td>92</td>
</tr>
<tr>
<td>18</td>
<td>R = Ph</td>
<td>3</td>
<td>94</td>
</tr>
<tr>
<td>19</td>
<td>X = O</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>20</td>
<td>X = S</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td>50 h</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$The aldehyde was treated with Ac$_2$O (1.5 equiv except for entries 6, 12–14) in the presence of Cu(BF$_4$)$_2$·xH$_2$O (1 mol%) under neat conditions at r.t.

$^b$Isolated yield of the corresponding 1,1-diacetate.

$^c$Except for entries 7, 11, and 13, all of the products were known and were clean (spectral analyses) and did not require any further purification. Wherever applicable, purification was performed through crystallization in n-hexane.

### Diacetoxy-1-(4-trifluoromethylphenyl)methane (Table 1, entry 7)

Mp 31–33 °C.

IR (neat): 1764 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.13$ (s, 6 H), 7.67 (s, 4 H), 7.76 (s, 1 H).

$^{13}$C NMR (300 MHz, CDCl$_3$): $\delta = 20.26$, 88.56, 121.83, 125.32, 125.36, 127.02, 131.19, 131.62, 139.18, 168.45.

Anal. Calcd for C$_{12}$H$_8$F$_6$O$_4$: C, 52.18; H, 4.01. Found: C, 52.15; H, 4.03.

### Diacetoxy(1-naphthyl)methane (Table 1, entry 11)

Mp 90–92 °C.

IR (KBr): 1760 cm$^{-1}$.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.13$ (s, 6 H), 7.44–7.59 (m, 3 H), 7.71 (d, $J = 6.9$ Hz, 1 H), 7.88–7.91 (m, 2 H), 8.24–8.27 (m, 2 H).

$^{13}$C NMR (300 MHz, CDCl$_3$): $\delta = 20.82$, 89.55, 124.06, 124.88, 126.00, 126.69, 127.68, 128.70, 130.22, 130.55, 133.89, 168.71.

Anal. Calcd for C$_{15}$H$_{12}$O$_4$: C, 69.47; H, 5.46. Found: C, 69.72; H, 5.47.

### Diacetoxy(2-methoxy-1-naphthyl)methane (Table 1, entry 13)

Mp 130–132 °C.

IR (KBr): 1752 cm$^{-1}$.
Copper(II) Tetrafluoroborate-Catalyzed Formation of Aldehyde-1,1-diacetates

1H NMR (300 MHz, CDCl3): δ = 2.09 (s, 6 H), 4.01 (s, 3 H), 7.26 (d, J = 8.3 Hz, 1 H), 7.36-7.41 (m, 1 H), 7.50–7.55 (m, 1 H), 7.79 (d, J = 8.0 Hz, 1 H), 7.87 (d, J = 9.1 Hz, 1 H), 8.42 (d, J = 8.6 Hz, 1 H), 8.66 (s, 1 H).

13C NMR (300 MHz, CDCl3): δ = 20.91, 57.29, 86.42, 113.68, 116.08, 123.82, 125.22, 126.87, 128.47, 129.45, 131.71, 132.26, 155.78, 168.73.


Acknowledgment
RT thanks CSIR, New Delhi, India, for the award of a Senior Research Fellowship.

References