Bismuth Triflate Catalyzed Allylation of Acetals: A Simple and Mild Method for Synthesis of Homoallyl Ethers

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Bismuth triflate catalyzed allylation of acetals: a simple and mild method for synthesis of homoallyl ethers

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Abstract—The allylation of acetals using allyltrimethylsilane is efficiently catalyzed by bismuth triflate (1.0 mol%). The reaction proceeds smoothly at room temperature to afford the corresponding homoallyl ether in good yield. The mild reaction conditions, the low toxicity of bismuth salts, and the high catalytic efficiency of the system make this procedure particularly attractive for large-scale synthesis.

Keywords: bismuth and compounds, allylation, homoallyl ethers, Lewis acid.

Of all the organic reactions, carbon–carbon bond forming reactions rank among the most important. Of particular interest is Lewis acid catalyzed carbon–carbon bond forming reactions since there is a wide range of selectivity and catalytic behavior among various Lewis acids. The allylation of acetals using organosilicon reagents has attracted much attention as a useful method to generate homoallyl ethers. Several catalysts have been used to effect this transformation. These include TiCl₄, AlCl₃, BF₃·Et₂O, trityl perchlorate, diphenylboryl triflate, montmorillonite, Pb/Al³⁺, trimethylsilyl bis(trifluorosulfonylimide), (CH₃)₃Si, TMSOTf, TiCp₂(CF₃SO₂)₂, CF₃COOH, BiBr₃, trimethylsilyl bis(trifluoromethanesulfonylimide) [TMSNTf₂], SC(OTf)₃, and indium metal. While most of these allylations require an activated alkene such as allyltrimethylsilane, other allyl group sources such as allyl bromide, lithium n-butyltriallylborate, and tetraallylltin have also been used. Several of these reagents suffer from certain drawbacks. Titanium trifluoroacetate is usually required in stoichiometric amounts and is quite corrosive and difficult to handle. Boron trifluoride etherate and aluminum chloride are especially corrosive while allyl bromide and tetraallylltin are both toxic. Furthermore, many of these methods require strictly anhydrous conditions and inconveniently low temperatures. With increasing environmental concerns, it is imperative that new “environment friendly” reagents be developed. Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis due to their low toxicity. We wish to report that bismuth triflate (1.0 mol%) is a very efficient catalyst for the allylation of acetals using allyltrimethylsilane (Scheme 1).

Bismuth triflate has previously been used as a catalyst for Friedel–Crafts acylations, sulfonylation of arenes, Diels–Alder reactions, aza-Diels–Alder reactions, rearrangement of epoxides, formation of acylals and deprotection of acetals. It is not commercially available but can be easily synthesized in the lab following a literature procedure. The experimental procedure of Scheme 1 is simple and the homoallyl ether product is obtained in high yield at room temperature. The results of this study are summarized in Table 1. Bismuth triflate is insoluble in common organic solvents and is used as a suspension. It is highly efficient and 1.0 mol% of bismuth triflate was sufficient to catalyze the allylation. Dichloromethane was found to be the best solvent for the rearrangement. The reaction works well with reagent grade dichloromethane that has not been dried or purified. Except in the case of acetophenone acetal (entry 9), no Scheme 1.
Table 1. Bismuth triflate catalyzed allylation of acetals in CH$_2$Cl$_2$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Time$^b$</th>
<th>Product</th>
<th>Yield$^{cd}$(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{PhOCH$_3$OCH$_3$}$</td>
<td>15 min</td>
<td>$\text{PhOCH$_3$}$</td>
<td>84$^{1a}$</td>
</tr>
<tr>
<td>2</td>
<td>$\text{OCH$_3$}$</td>
<td>15 min</td>
<td>$\text{OCH$_3$}$</td>
<td>69$^{c, 13}$</td>
</tr>
<tr>
<td>3</td>
<td>$\text{OCH$_2$CH$_3$}$</td>
<td>10 min</td>
<td>$\text{OCH$_2$CH$_3$}$</td>
<td>88$^{e}$</td>
</tr>
<tr>
<td>4</td>
<td>$\text{OCH$_3$}$</td>
<td>5 min</td>
<td>$\text{OCH$_3$}$</td>
<td>96$^{g}$</td>
</tr>
<tr>
<td>5</td>
<td>$\text{OCH$_3$}$</td>
<td>1.5 h</td>
<td>$\text{OCH$_3$}$</td>
<td>94$^{f}$</td>
</tr>
<tr>
<td>6</td>
<td>$\text{OCH$_3$}$</td>
<td>15 min</td>
<td>$\text{OCH$_3$}$</td>
<td>84$^{1b}$</td>
</tr>
<tr>
<td>7</td>
<td>$\text{CH$_3$}$</td>
<td>40 min</td>
<td>$\text{OCH$_3$}$</td>
<td>73$^{6}$</td>
</tr>
<tr>
<td>8</td>
<td>$\text{MeO}$</td>
<td>1 h</td>
<td>$\text{MeO}$</td>
<td>82$^{3a}$</td>
</tr>
<tr>
<td>9</td>
<td>$\text{MeO}$</td>
<td>4-20 h</td>
<td>$\text{MeO}$</td>
<td>Variable (see foot note f)</td>
</tr>
<tr>
<td>10</td>
<td>$\text{OCH$_3$}$</td>
<td>21 h</td>
<td>NR$^{g}$</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>$\text{PhOCH$_3$OCH$_3$}$</td>
<td>16 h</td>
<td>NR$^{g}$</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Although all reactions were run in anhydrous CH$_2$Cl$_2$, reactions typically also work well with reagent grade CH$_2$Cl$_2$. Conditions: 1.0 mol % bismuth triflate and 1.3 equivalents of allyltrimethylsilane at room temperature.

$^b$Reaction progress was followed by GC or TLC.

$^c$Refers to yield of isolated product. Crude product was found to be ≥ 96 % pure by GC, $^1$H NMR and $^{13}$C NMR analysis. All products (except that from entry 3) have been previously reported in the literature.

$^d$Superscript against yield refers to literature reference for product.

$^e$Refers to yield of pure product (> 98 %) after purification by flash column chromatography.

$^f$For reactions with acetylphenone acetal, bismuth triflate was dried at 65 °C and 0.1 mm Hg and stored in a desiccator. Allyltrimethylsilane was dried over Na$_2$SO$_4$ and distilled and dispensed under N$_2$.

$^g$Starting material was recovered in good yield.
carbonyl compound was detected by $^1$H NMR spectroscopy of the crude product. This observation suggests that bismuth triflate catalyzed allylation is significantly faster than deprotection of acetal by any water present in the solvent. This is a significant advantage over other methods that require the use of strictly anhydrous conditions. When the allylation of benzaldehyde dimethyl acetal (entry 1) was done neat, in addition to the desired product, considerable amounts of impurities were formed. The procedure works well with a wide variety of acetals including acetals derived from conjugated aldehydes (entry 6). It has been reported that with TiCl$_4$ as the activator, the reaction of cinnamaldehyde dimethyl acetal gave only the diallylated product. Even at low temperatures ($-78^\circ$C), the monoallylated product was not formed. Similar results were obtained when allylation of cinnamaldehyde dimethylacetal was carried out using allyltrimethylsilane. However, no acetophenone was formed. The authors wish to acknowledge funding by the National Science Foundation (RUI grant). R.M. would also like to acknowledge The Camille and Henry Dreyfus Foundation for a research award. We would also like to thank Professor Jacques Dubac, Universite Paul Sabatier, France for useful discussions.

In summary, this work demonstrates a new method for high-yielding allylation of acetals using catalytic amounts of Bi(OTf)$_3$. Advantages of this method include fast reaction rates and the use of a Lewis acid that is highly catalytic in nature, is relatively inexpensive, non-toxic and insensitive to small amounts of air and moisture.

Acknowledgements

The authors wish to acknowledge funding by the National Science Foundation (RUI grant). R.M. would also like to acknowledge The Camille and Henry Dreyfus Foundation for a research award. We would also like to thank Professor Jacques Dubac, Universite Paul Sabatier, France for useful discussions.

References

27. **Representative procedure:** A solution of 3-bromobenzaldehyde diethyl acetal (0.500 g, 1.93 mmol) and allyltrimethylsilane (0.286 g, 2.51 mmol) in CH₂Cl₂ (5 mL) was stirred as Bi(OTf)₃·xH₂O (12.7 mg, 0.0194 mmol, 1 mol%) was added. After 10 min aqueous 10% Na₂CO₃ (10 mL) was added and the mixture was stirred well. The layers were separated, and the aqueous layer was extracted again with CH₂Cl₂ (2×20 mL). The combined organic layers were washed with saturated NaCl (25 mL), dried (Na₂SO₄) and concentrated on a rotary evaporator to give 0.436 g (88%) of a colorless liquid that was determined to be >98% pure by GC, ¹H and ¹³C NMR spectroscopy. A small sample was purified further for elemental analysis. ¹H NMR: δ (CDCl₃, 270 MHz): 1.17 (t, 3H, J=6.93 Hz), 2.44 (doublet of pentets, 2H), 3.33 (m, 2H), 4.21 (t, 1H, J=6.5 Hz), 5.03 (m, 2H), 5.75 (m, 1H), 7.30 (m, 4H). ¹³C (67.5 MHz) 15.2, 42.5, 64.3, 81.1, 117.1, 122.4, 125.1, 129.6, 129.8, 130.4, 134.3, 144.9. Anal. calcd for C₁₂H₁₅BrO: C, 56.49; H, 5.93; Br, 31.32. Found: C, 56.73; H, 6.00, Br, 31.44%.