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

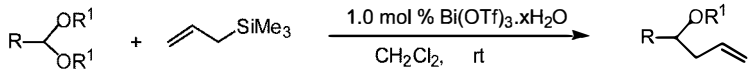
Laura C. Wieland, Herbert M. Zerth and Ram S. Mohan

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.

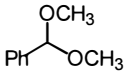
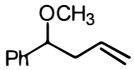
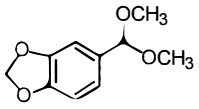
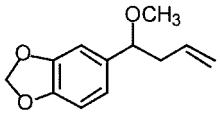
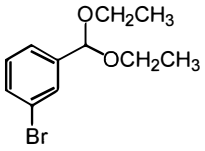
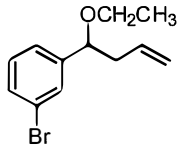
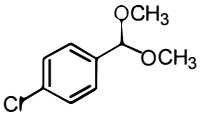
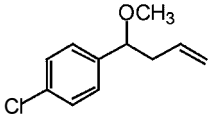
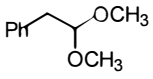
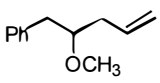
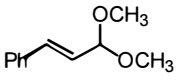
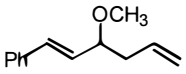
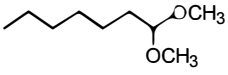
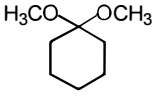
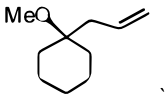
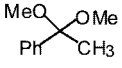
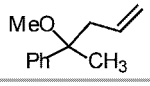
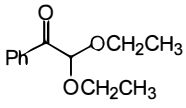
Of all the organic reactions, carbon–carbon bond forming reactions rank among the most important. Of particular interest is Lewis acid catalyzed carbon–carbon bond forming reactions since there is a wide range of selectivity and catalytic behavior among various Lewis acids. The allylation of acetals 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 $TiCl_4$,[1] $AlCl_3$,[2] $BF_3{\cdot}Et_2O$,[2] trityl perchlorate,[3] diphenylboryl triflate,[3] montmorillonite,[4] Pb/Al,[5] trimethylsilyl bis(fluorosulfonyl)imide,[6] $(CH_3)_4SiI$,[7] TMSOTF,[8] $TiCp_2(CF_3SO_3)_2$,[9] CF_3COOH,[10] $BiBr_3$,[11] trimethylsilyl bis(trifluoromethanesulfonyl)amide [$TMSNTf_2$],[12] $Sc(OTf)_3$,[13] and indium metal.[14] While most of these allylations require an activated alkene such as allyltrimethylsilane, other allyl group sources such as allyl bromide,[2] lithium *n*-butyltriallylborate,[15] and tetraallyltin[10] have also been used. Several of these reagents suffer from certain drawbacks. Titanium tetrachloride 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 tetraallyltin 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.[16] Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis due to their low toxicity.[17,18] 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,[19] sulfonylation of arenes,[20] Diels–Alder reactions,[21] aza-Diels–Alder reactions,[22] rearrangement of epoxides,[23] formation of acylals[24] and deprotection of acetals.[25] It is not commercially available but can be easily synthesized in the lab following a literature procedure.[26] The experimental procedure of Scheme 1 is simple and the homoallyl ether product is obtained in high yield at room temperature.[27] 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_2Cl_2[a]

Entry	Substrate	Time[b]	Product	Yield[c,d](%)
1		15 min		84[1a]
2		15 min		69[e, 13]
3		10 min		88[e]
4		5 min		96[5]
5		1.5 h		94
6		15 min		84[1b]
7		40 min		73[6]
8		1 h		82[1a]
9		4-20 h		Variable (see foot note f)
10		21 h	NR[g]	
11		16 h	NR[g]	

[a] Although all reactions were run in anhydrous CH_2Cl_2, reactions typically also work well with reagent grade CH_2Cl_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, ^1H 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 acetophenone acetal, bismuth triflate was dried at 65 °C and 0.1 mm Hg and stored in a desiccator. Allyltrimethylsilane was dried over Na_2SO_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 with allyltrimethylsilane gave only the diallylated product.[2] Even at low temperatures (−78°C), the monoallylated product was not formed. Similar results were obtained when allylation of cinnamaldehyde dimethylacetal was carried out using allyl bromide in the presence of $AlBr_3$.[5] In contrast, we did not observe any diallylated product using bismuth triflate as the catalyst and the monoallylated product was obtained in good yields in all cases.

The allylation of acetophenone dimethyl acetal (entry 9) was found to be very slow under the reaction conditions. The use of reagent grade CH_2Cl_2 also resulted in the formation of considerable amounts of acetophenone. Thus it appears that the deprotection of acetophenone acetal catalyzed by bismuth triflate is faster than the corresponding allylation. Consistent with these results is the observation that when acetophenone acetal (in the absence of allyltrimethylsilane) was stirred as a solution in reagent grade CH_2Cl_2 in the presence bismuth triflate (1.0 mol%), acetophenone was obtained in good yield. Hence the allylation was carried out neat using pre-dried allyltrimethylsilane and dry bismuth triflate. The reaction was only 50% complete after 18 h using 1.0 mol% bismuth triflate and 1.3 equiv. of allyltrimethylsilane. However, no acetophenone was formed under these reaction conditions. The use of 5.0 mol% bismuth triflate did not accelerate the reaction considerably. When the reaction was carried out with 1.0 mol% bismuth triflate and 4 equiv. of allyltrimethylsilane, the reaction was 60% complete. In contrast, the use of 2 mol% triflic acid resulted in >90% completion. When the reaction was carried out using 5 mol% bismuth triflate and 4.0 equiv. of allyltrimethysilane, no SM was present after 5 h. However ^{1}H NMR analysis of the product indicated that it was a mixture of the desired product and diallylated product. This mixture was inseparable by column chromatography. Similar diallylation was observed when the allylation was attempted using 1.3 equiv. of allyltrimethylsilane and 1.0 mol% bismuth triflate at 60°C.

No allylation was observed in the case of 2,2-diethoxyacetophenone (entry 10). While many examples of allylation of aldehydes have been reported in the literature,[28] under the conditions used, the allylation of benzaldehyde (entry 11) was found to be extremely slow. Even after 24 h less than 5% allylation occurred and the unreacted benzaldehyde was recovered in good yield.

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.

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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 CH_2Cl_2 (5 mL) was stirred as $Bi(OTf)_3 \cdot xH_2O$ (12.7 mg, 0.0194 mmol, 1 mol%) was added. After 10 min aqueous 10% Na_2CO_3 (10 mL) was added and the mixture was stirred well. The layers were separated, and the aqueous layer was extracted again with CH_2Cl_2 (2×20 mL). The combined organic layers were washed with saturated NaCl (25 mL), dried (Na_2SO_4) 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 ^{13}C NMR spectroscopy. A small sample was purified further for elemental analysis. ^1H NMR: δ ($CDCl_3$, 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). ^{13}C (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 $C_{12}H_{15}BrO$: C, 56.49; H, 5.93; Br, 31.32. Found: C, 56.73; H, 6.00, Br, 31.44%.
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