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An efficient method for the chemoselective synthesis of acylals from aromatic aldehydes using bismuth triflate

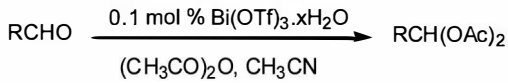
Marc D. Carrigan, Kyle J. Eash, Matthew C. Oswald and Ram S. Mohan

Abstract—Aromatic aldehydes are smoothly converted into the corresponding acylals in good yields in the presence of 0.10 mol% $Bi(OTf)_3 \cdot xH_2O$. Ketones are not affected under the reaction conditions. The highly catalytic nature of bismuth triflate and the fact that it is relatively non-toxic, easy to handle and insensitive to small amounts of air and moisture makes this procedure especially attractive for large-scale synthesis.

Keywords: acylals, acylation, bismuth and compounds, protecting groups.

Acylals (geminal diacetates) have often been used as protecting groups for carbonyl compounds because they are stable to neutral and basic conditions.[1,2] Hence, methods for their synthesis have received considerable attention. Some of the reagents and catalysts that have been developed for this purpose include sulfuric acid,[2] triflic acid,[3] PCl_3,[4] TMSCl–NaI,[5] $ZnCl_2$,[6] I_2,[7] anhydrous ferrous sulfate,[8] $FeCl_3$,[9] and NBS.[10] Several inorganic heterogeneous catalysts have also been developed as catalysts for synthesis of acylals.[11] Lewis acids such as $Cu(OTf)_2$ (2.5 mol%)[12] and $Sc(OTf)_3$ (2 mol%)[13] are also efficient for this conversion. Many of these reagents are highly corrosive and difficult to handle while copper and scandium triflate are rather expensive. Recently, bismuth compounds have attracted attention because of their low toxicity, low cost and relative insensitivity to air and small amounts of moisture.[14] In a recent study aimed at investigating bismuth triflate catalyzed acetylations of phenols, we observed that when 4-hydroxybenzaldehyde was reacted with acetic anhydride in the presence of $Bi(OTf)_3 \cdot xH_2O$, not only was the phenol converted to the corresponding acetate but the aldehyde moiety was also converted to the corresponding acylal. This observation prompted us to investigate the utility of bismuth triflate as a catalyst for conversion of aldehydes to acylals.

We wish to report that bismuth triflate is a highly efficient catalyst for the conversion of aromatic aldehydes to acylals (Scheme 1).

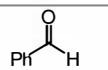
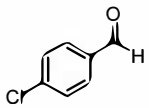
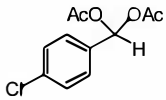
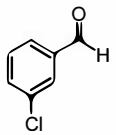
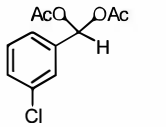
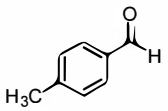
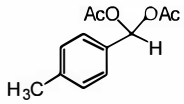
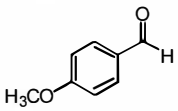
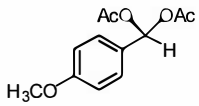
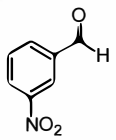
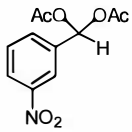
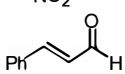
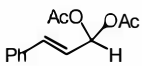
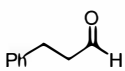
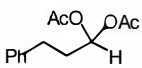
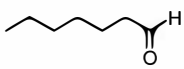
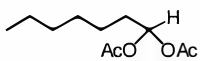
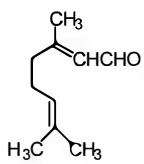
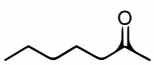
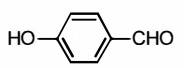
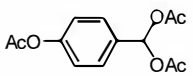
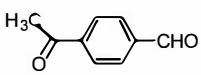
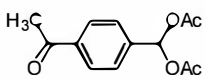


Scheme 1.

Bismuth triflate, $Bi(OTf)_3 \cdot xH_2O$ is much more efficient than $Sc(OTf)_3$ and $Cu(OTf)_2$ as a catalyst for this conversion. Only 0.1 mol% of $Bi(OTf)_3 \cdot xH_2O$ is needed to effect reaction. We recently reported the use of bismuth triflate as a catalyst for rearrangement of epoxides to aldehydes and ketones.[15] Bismuth triflate has also been used as a catalyst for Friedel–Crafts acylations,[16] sulfonylations,[17] Diels–Alder reactions,[18] and aza-Diels–Alder reactions.[19] Although $Bi(OTf)_3$ is not commercially available it can be easily synthesized as the tetrahydrate at a relatively low cost.[20] The experimental procedure for synthesis of acylals is straightforward and involves stirring the aldehyde and acetic anhydride as a solution in acetonitrile.[21] A wide variety of aromatic aldehydes underwent smooth reaction to give the corresponding acylal in good yield (Table 1). It should also be noted that this reaction can be carried out under solvent free conditions.[22]

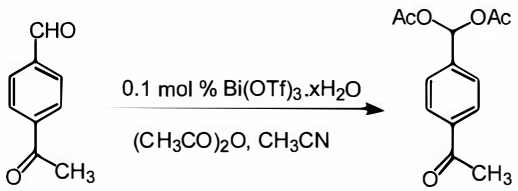
Aliphatic aldehydes (entries 8–10) reacted sluggishly in acetonitrile but rapid reaction occurred under solvent free conditions. However, the product yield was lower than those obtained with aromatic aldehydes. We attribute the lower yield to the formation of some unidentifiable by-products. ^1H and ^{13}C NMR spectral analysis of the crude product from aliphatic aldehydes (entries 8 and 9) showed peaks in the olefininc region, but the by-products were not consistent with the corre-

Table 1. Formation of acylals from aldehydes using $Bi(OTf)_3 \cdot xH_2O$

Entry[a]	Substrate	Method[b]	Time	Product	Yield (%)[c]
1[9a]		A	45 min		91[d]
		B	20 min		88[d]
2[23]		A	2 h		85[d]
		B	40 min		92[d]
3[24]		A	2 h		84[d]
		B	35 min		90[d]
4[9a]		A	3.5 h		87[d]
		B	30 min		85[d]
5[23]		A	4 h		83[e]
6[9a]		A	4.5 h		88[d]
		B	1.5 h		95[d]
7[9a]		A	2 h		79[f]
		B	15 min		70[f]
8[9a]		A	4 h		see note h
		B	10 min		90[e]
9[25]		A	5 h		see note h
		B	10 min		64[e]
10		A	2 h	NR	
11		A[g]	12 h	NR	
12		B[g]	17 h	NR	
13[26]		B	20 min		98
14[27]		A	2 h		98

[a] Superscript against entry # refers to literature reference for product.
[b] *Method A*: 3 equiv. of $(CH_3CO)_2O$, CH_3CN, 0.1 mol% $Bi(OTf)_3 \cdot xH_2O$. *Method B*: 1.5 equiv. of $(CH_3CO)_2O$, no solvent, 0.1 mol% $Bi(OTf)_3 \cdot xH_2O$.
[c] Refers to yield of isolated product.
[d] Crude product was estimated to be >98% by ^1H and ^{13}C NMR spectroscopy and GC analyses, and hence it was not purified further.
[e] Purified by flash column chromatography.
[f] Purified by recrystallization from hexanes.
[g] Reaction carried out under reflux.
[h] After 5 h at room temperature, less than 10% conversion to product had occurred.

sponding enol acetates that would result if the acylal underwent an elimination reaction. Ketones proved resistant to the reaction conditions and no diacetate formed even under reflux conditions. The chemoselectivity of this method was demonstrated using acetylbenzaldehyde (entry 14). Smooth conversion of the aldehyde to the diacetate was observed while the ketone functionality remained unaffected (Scheme 2).



Scheme 2.

In summary, a new highly catalytic and chemoselective method has been developed for conversion of aromatic aldehydes to acylals using bismuth triflate. Advantages of this method include: (1) the use of an inexpensive and relatively non-toxic catalyst (2) high catalytic efficiency and (3) the observed chemoselectivity.

Acknowledgements

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21. *Method A*: A solution of benzaldehyde (5.00 g, 0.0471 mol) in acetonitrile (15 mL) was stirred as acetic anhydride (14.44 g, 0.141 mol) and $Bi(OTf)_3 \cdot xH_2O$ (31 mg, 4.71×10^{-5} mol) were added. The reaction progress was monitored by TLC. After 45 min, 10% $NaHCO_3$ (15 mL) was added and the mixture was stirred for 5 min. The mixture was extracted with ether (2×40 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ until basic, H_2O (2×25 mL), saturated NaCl (25 mL) and dried (Na_2SO_4). The solvents were removed on a rotary evaporator to give 8.91 g (91%) of benzylidene diacetate that was determined to be 98% pure by ^1H and ^{13}C NMR and GC analysis. *Method B*: A solution of the aldehyde in acetic anhydride was stirred and cooled in an ice bath to −5°C as bismuth triflate was added. Work up was carried out as described under method A.
22. *Caution*: An exothermic reaction ensues upon addition of bismuth triflate. Adequate care must be exercised, especially if this reaction is scaled up.
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26. The product has been reported before (Ref. 11e) but spectral data were not given. ^1H NMR (270 MHz, $CDCl_3$): δ 2.11 (s, 6H), 2.29 (s, 3H), 7.11 (d, 2H, $J=8.6$ Hz), 7.53 (d, 2H, $J=8.6$ Hz), 7.66 (s, 1H). ^{13}C NMR ($CDCl_3$, 67.5 MHz) 20.62, 20.87, 88.94, 121.66, 127.87, 132.88, 151.40, 168.53, 169.04.
27. Data for the product is reported here. ^1H NMR (270 MHz, $CDCl_3$): δ 2.12 (s, 6H), 2.60 (s, 3H), 7.60 (d, 2H, $J=8.4$ Hz), 7.69 (s, 1H), 7.98 (d, 2H, $J=8.4$ Hz). ^{13}C (67.5 MHz, $CDCl_3$): 20.68, 26.60, 88.86, 126.84, 128.46, 137.90, 139.88, 168.55, 197.34. Mp: 56–59°C. Anal. calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.28; H, 5.48.