$Sc(OTf)_3$, an Efficient Catalyst for Formation and Deprotection of Geminal Diacetates (Acylals); Chemoselective Protection of Aldehydes in Presence of Ketones

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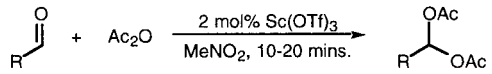
Abstract: Scandium triflate (2 mol%) has been found to be an extremely efficient catalyst for the addition of acetic anhydride to both aromatic and aliphatic aldehydes. Deprotection of the resulting geminal diacetates (acylals) was achieved using the same catalyst in the presence of water.

Acylals[1] have been reported as efficient protecting groups for aldehydes as they are stable in neutral and basic media.[2] Typically, they are synthesised from acetic anhydride and aldehydes using strong Brönsted acids as catalysts (typically sulfuric acid[1] or Nafion-H[3]) or Lewis acids (e.g. $FeCl_3$,[2] $ZnCl_2$[4] or PCl_3[5]) but these methods are often accompanied by long reaction times or low yields. More recently, zeolites[6] and iodine[7] have also been shown to be efficient catalysts for this reaction.

During the course of investigations into Lewis acid catalysed additions to benzaldehyde with a range of nucleophiles,[8] we found that scandium triflate catalysed the formation of the corresponding acylal, both cleanly and efficiently.[9] To probe the generality of this process, a range of both aromatic, unsaturated and aliphatic aldehydes were screened in this reaction (Table).

Table . Scandium Triflate Catalysed Acylal Formation

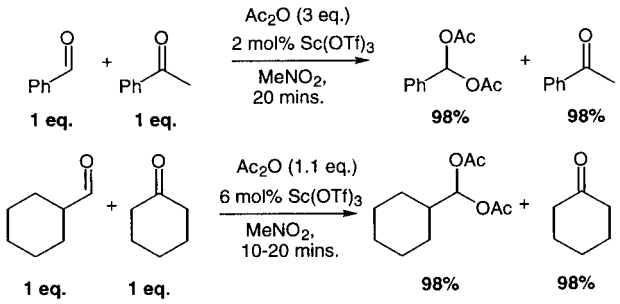


Entry	Aldehyde	Time /mins	Isolated Yield/%
1	4-Nitrobenzaldehyde	10	99
2	4-Chlorobenzaldehyde	10	95
3	Benzaldehyde	10	99
4	4-Methylbenzaldehyde	10	95
5	4-Methoxybenzaldehyde	20	45[a]
6	Cinnamaldehyde[b]	120	76
7	Cyclohexanecarboxaldehyde	20	94

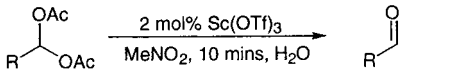
[a] The remainder (55%) is recovered aldehyde. [b] A different batch of catalyst was used which may account for the longer reaction time

We were pleased to find that both activated and weakly deactivated aromatic aldehydes (entries 1-4) gave the corresponding acylals in near quantitative yield after chromatographic purification. Aliphatic aldehydes also reacted efficiently (entry 7). Highly deactivated aromatic aldehyde (entry 5) gave a lower yield of the protected aldehyde, with the remainder of the material recovered as unreacted aldehyde.

Ketones (cyclohexanone, acetophenone) did not give any acylals under the same reaction conditions and this suggested that chemoselective protection of an aldehyde in the presence of a ketone could be achieved. This was shown to be the case in the examples given.



Additionally, treatment of the acylals derived from benzaldehyde and cyclohexanecarboxaldehyde with water in the presence of scandium triflate gave a high yield of deprotected aldehyde.



Typical Experimental Procedure for the Formation of Acylals: To a stirred solution of scandium triflate (9.8 mg, 0.02 mmol) and benzaldehyde (102 μL, 1.0 mmol) in nitromethane (10 mL) at room temperature was added dropwise acetic anhydride (142 μL, 1.5 mmol). The mixture was stirred at room temperature until complete consumption of the aldehyde was achieved (as monitored by tlc). Concentration *in vacuo* and chromatography (10% EtOAc/Petrol; silica gel) gave the product as a white solid (206 mg, 0.99 mmol, 99%), R_f 0.26 (10% EtOAc/Petrol); mp 43-45°C [Lit.,[5] mp 44-46 °C]; δ_H(250 MHz; $CDCl_3$) 2.12 (6 H, s, CH_3), 7.39-7.43 (3 H, m, ArH), 7.50-7.54 (2 H, m, ArH) and 7.68 (1 H, s, CH).

Experimental Procedure for the Deprotection of Acetic Acid Acetoxy Phenyl Methyl Ester: To a stirred solution of acetic acid acetoxy phenyl methyl ester (104 mg, 0.5 mmol) in nitromethane (0.5 mL) was added scandium triflate (4.9 mg, 0.01 mmol) and water (9 μL, 0.5 mmol). The mixture was stirred at room temperature for 10 mins. Concentration *in vacuo* and chromatography (10% EtOAc/Petrol; silica gel) gave benzaldehyde (50 mg, 0.47 mmol, 94%).

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