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POLYSTYRENE-SUPPORTED, Al(OTf)$_3$-CATALYZED CHEMOSELECTIVE SYNTHESIS OF ACYLALS FROM ALDEHYDES

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Cross-linked polystyrene-supported aluminium triflate [Ps-Al(OTf)$_3$] has been shown to be a mild, efficient, and chemoselective heterogeneous Lewis acid catalyst for acetylation of aldehydes with acetic anhydride. The catalyst can be recovered simply and reused efficiently at least five times without any noticeable loss of catalytic activity.

Keywords: Acylal; aldehyde; aluminium triflate; catalysis; polystyrene

INTRODUCTION

The application of heterogeneous catalysts in place of homogeneous catalysts in organic synthesis is an attractive area of research in the laboratory as well as in the industrial context.[1] Such heterogeneous catalysts are as active as their homogeneous counterparts while having the distinguishing characteristics of being easily separable from reaction media, ease of handling, stability (toward air and moisture), lack of corrosion, recyclability, and selectivity in various organic reactions. Although the use of heterogeneous acid catalysts is of continuing interest, few examples are known for polymer-supported Lewis acid catalysts.[2]

Acylals have attracted great interest in organic synthesis for the protection of carbonyl groups because of their remarkable stability in basic and neutral reaction media as well as toward aqueous acids.[3] In addition, acylals are important synthons and useful precursors in organic chemistry. They can be used as cross-linking reagents for cellulose in cotton[4] and are important starting materials for the synthesis of valuable intermediates in Diels–Alder reactions,[5] carbonyl surrogates for asymmetric synthesis,[6] and substrates for nucleophilic substitution reactions.[7,8] Generally, acylals can be prepared from aldehydes by treatment with acetic anhydride in the presence of a suitable catalyst such as proton acids (e.g., H_2SO_4, CH_3SO_3H, NH_2SO_3H, and *p*-toluene sulfonic acid),[9–12] Lewis acids (e.g., $FeCl_3$, $AlCl_3$, WCl_6, $ZrCl_4$, $In(OTf)_3$, $Sc(OTf)_3$, $Bi(OTf)_3 \cdot xH_2O$, and $RuCl_3 \cdot xH_2O$),[13–20] heteropoly acids (e.g., 12-molybdophosphoric acid),[21] solid acidic catalysts (e.g., nafion-H, Fe^{3+}-montmorillonite, amberlyst-15, $InCl_3/Al_2O_3$, $HClO_4/SiO_2$, and

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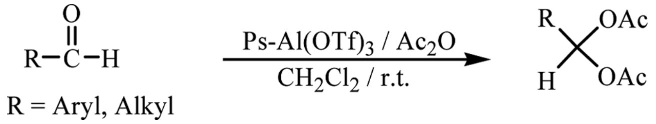


Scheme 1. Acetylation of aldehydes with Ac_2O using Ps-Al$(OTf)_3$.

$H_3PW_{12}O_{40}$-supported MCM-41 molecular sieves),[22–27] and ionic liquids.[28] However, most of these methods suffer from one or more disadvantages such as long reaction times, high reaction temperature, strongly acidic or oxidizing conditions, poor selectivity, tedious workup, disturbance to other functional groups, environmental pollution, use of stoichiometric or excess amounts of catalyst, or the use of moisture-sensitive, expensive, or unreusable catalysts. In view of these, the search for finding a cost-effective, mild, and simple chemoselective protocol for the synthesis of acylals is still relevant.

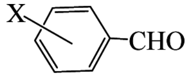
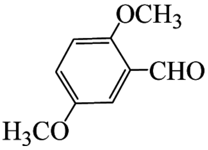
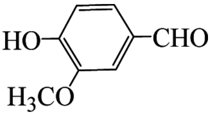
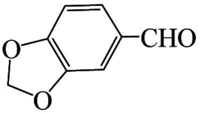
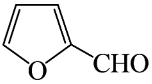
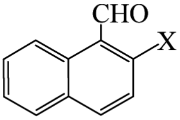
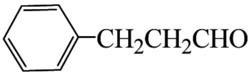
In continuation of our ongoing program to develop environmentally benign methods using heterogeneous catalysts,[29–31] we reported Ps-Al$(OTf)_3$ as a new polymeric Lewis acid catalyst for dithioacetalization of carbonyl compounds and transdithioacetalization of acetals.[32] Along this line, we now report that Ps-Al$(OTf)_3$ is also an effective and highly chemoselective heterogeneous catalyst for acetylation of aldehydes with acetic anhydride under mild reaction conditions (Scheme 1).

RESULTS AND DISCUSSION

Ps-Al$(OTf)_3$ was prepared by the exchange reaction between cross-linked polystyrene-supported aluminium chloride (Ps-$AlCl_3$) and triflic acid in freon 113 under reflux conditions. The capacity of the catalyst obtained by the gravimetric method and checked by atomic absorption was 0.41 mmol Al$(OTf)_3$ per gram. Using this catalyst, various aldehydes (aromatic, aliphatic, and α,β-unsaturated aldehydes) were converted into their corresponding acylals in good to excellent yields at room temperature in dichloromethane, which proved to be the solvent of choice among other organic solvents (Table 1, entries 1–10). The optimum molar ratio of Ps-Al$(OTf)_3$ to aldehyde was found to be 0.1:1. In the case of 2-hydroxybenzaldehyde and vanillin, both carbonyl and phenolic-OH groups were acetylated when excess acetic anhydride was used (entries 1i and 3). The acid-sensitive substrate furfural also led to the formation of the corresponding acylal in 94% yield without the formation of any side products, which are normally encountered under acidic conditions (entry 5). 4-(Dimethylamino) benzaldehyde failed to give the corresponding acylal under the same reaction conditions, possibly due to tautomerization and the existence of the quininoid structure (entry 1j).[23] However, ketones did not produce the corresponding diacetates under the same reaction conditions (entries 11–13). Ps-Al$(OTf)_3$ is stable under the reaction conditions, and there is no leaching of acid moieties during reactions.

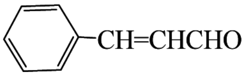
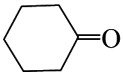
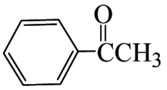
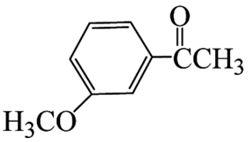
To evaluate the selectivity of this method, we investigated competitive reactions using Ps-Al$(OTf)_3$, Al$(OTf)_3$, and $AlCl_3$ for acetylation of aldehydes in the presence

Table 1. Conversion of aldehydes into acylals catalyzed by Ps-Al(OTf)$_3$[a,b]

				Mp (°C) or Bp (°C/torr)	
Entry	Aldehyde	Time (h)	Yield (%)	Found	Reported
1					
	a. X = H	1	94	44–46	43–44[14]
	b. X = 4-CH_3	1	94	82–83	81–82[23]
	c. X = 4-OCH_3	1	94	65–67	67–68[14]
	d. X = 4-Cl	1.1	94	80	81[27]
	e. X = 3-NO_2	1.3	95	63–65	62–64[14]
	f. X = 4-NO_2	1.25	94	125	124[14]
	g. X = 4-Ph	1.1	93	127–129	128–130[16]
	h. X = 4-OCH_2Ph	1.5	95	107–109	108–110[26]
	i. X = 2-OH	2.1	94	105	104[27]
	j. X = 4-$N(CH_3)_2$	6	—	—	—
2		0.9	95	53–55	52[27]
3		2.1	90	91	90–91[26]
4		1.1	92	78–79	77–78[17]
5		1.15	94	50–51	50–51[23]
6					
	a. X = H	2.2	91	109	110[27]
	b. X = OCH_3	2.1	92	134–136	133–135[16]
7		1.5	89	Oil	185–190/0.7[13]
8	$CH_3(CH_2)_nCHO$				
	a. n = 4	1.15	91	Oil	Oil[26]
	b. n = 5	1.5	90	135–137/2	136–137/2[14]
	c. n = 6	1.6	90	Oil	Oil[17]

(*Continued*)

Table 1. Continued

				Mp (°C) or Bp (°C/torr)	
Entry	Aldehyde	Time (h)	Yield (%)	Found	Reported
9		2	91	84–86	83–85[20]
10	$CH_3CH{=}CHCHO$	1.8	90	91–93/15	90–91/15[14]
11		8	—	—	—
12		8	—	—	—
13		8	—	—	—

[a]The molar ratio of the aldehyde/Ac_2O/cat. is 1:1.5:0.1 except for entries **1i** and **3**, in which the molar ratio is 1:2.5:0.12.

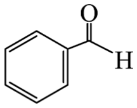
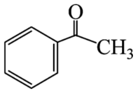
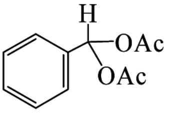
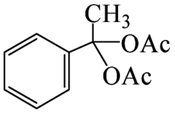
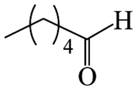
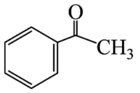
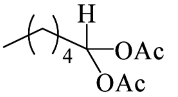
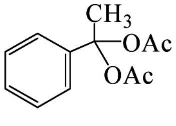
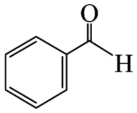
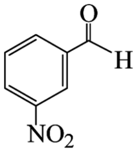
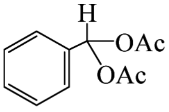
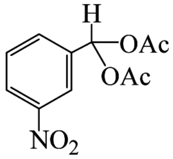
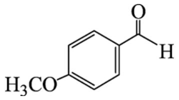
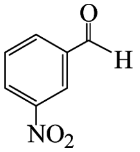
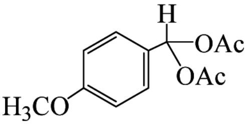
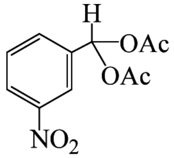
[b]Yields refer to pure isolated products, and all acylals prepared are known compounds and were characterized by comparison of their physical and spectral data with those of authentic samples.

of ketones (Table 2, entries 1 and 2) and more important, selective acetylation of benzaldehyde and 4-methoxybenzaldehyde versus 3-nitrobenzaldehyde (entries 3 and 4). From the results, it is clear that very high chemoselectivity was observed in the presence of Ps-Al(OTf)$_3$ and that this catalyst shows greater chemoselectivity than Al(OTf)$_3$ and $AlCl_3$ in acetylation reactions. Moreover, Al(OTf)$_3$ and $AlCl_3$ might be required in reagent quantities as a consequence of their ability to strongly complex Lewis base products. The observed high chemoselectivity of acetylation reactions is presumably a result of mild catalytic activity of Ps-Al(OTf)$_3$, difference in steric bulkiness of the carbonyl compounds, and also the influence of electronic effects upon these reactions in the presence of Ps-Al(OTf)$_3$. The present chemoselectivities can be suitable for acetylation of aldehydes for the synthesis of complex molecules by multistep processes.

It is important to note that Ps-Al(OTf)$_3$ shows greater catalytic activity than Ps-$AlCl_3$ in acetylation reactions (Scheme 2).

In conclusion, Ps-Al(OTf)$_3$ is an efficient and convenient polymer-supported Lewis acid catalyst for acetylation of aldehydes. This catalyst has comparable activity with $AlCl_3$ and Al(OTf)$_3$, but it has added advantages involving its ability to be recycled, nontoxicity, noncorrosiveness, ease of handling (as a benchtop catalyst), and high chemoselectivity. Good yields, green and mild reaction conditions, facile workup, and short reaction times are other notable features of this protocol. Further investigations to apply Ps-Al(OTf)$_3$ are now in progress.

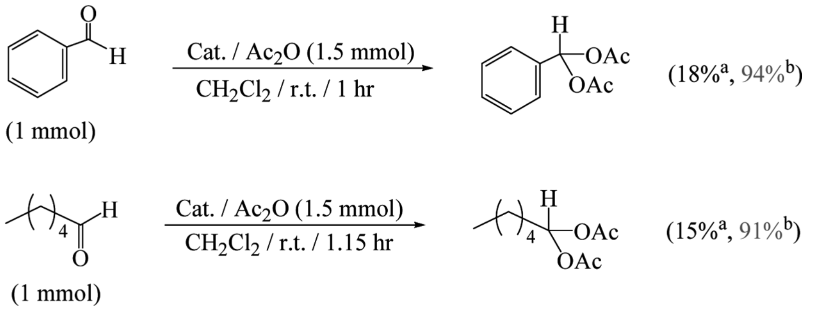
Table 2. Competitive acylal formation reactions using Ac_2O in the presence of Ps-Al(OTf)$_3$, Al(OTf)$_3$, and $AlCl_3$^{a,b}

Entry	Substrate 1	Substrate 2	Product **1** yield (%)^{c}	Product **2** yield (%)^{c}	Time (h)
1			 (94%,^{1} 88%,^{2} 80%^{3})	 (0%,^{1} 8%,^{2} 7%^{3})	1.1
2			 (91%,^{1} 88%,^{2} 78%^{3})	 (0%,^{1} 8%,^{2} 8%^{3})	1.2
3			 (93%,^{1} 62%,^{2} 60%^{3})	 (7%,^{1} 34%,^{2} 38%^{3})	1.15
4			 (92%,^{1} 63%,^{2} 62%^{3})	 (8%,^{1} 37%,^{2} 36%^{3})	1.1

[a] The molar ratio of substrate 1 to substrate 2 to Ac_2O is 1:1:1.2 for entries 1 and 2 and 1:1:1 for entries 3 and 4.

[b] All reactions were carried out in CH_2Cl_2 at room temperature in the presence of ^{1}Ps-Al(OTf)$_3$ (0.1 mmol), ^{2}Al(OTf)$_3$ (0.2 mmol), or $^{3}AlCl_3$ (0.28 mmol).

[c] GC yield.



Scheme 2. Catalyst a: Ps-$AlCl_3$ (0.35 mmol); b: Ps-Al(OTf)$_3$ (0.1 mmol).

EXPERIMENTAL

Materials and Techniques

Chemicals were either prepared in our laboratory or were purchased from Merck and Fluka. Polystyrene (8% divinylbenzene, prepared via suspension polymerization, polyvinylpyrrolidone 90 K as suspension agent, grain size range: 0.25–0.6 mm) was obtained from Iran Polymer and Petrochemical Institute. Infrared (IR) spectra were run on a Shimadzu model 8300 Fourier transform (FT)–IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300-MHz) spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as the internal standard. Capacity of the catalyst was determined by the gravimetric method and atomic absorption technique using a Philips atomic absorption instrument. Melting points were determined on a Fisher-Jones melting-point apparatus and are uncorrected. Reaction monitoring and purity determination of the products were accomplished by GLC or thin-layer chromatography (TLC) on commercial plates of silica gel GF_{254}.

Preparation of Ps-Al(OTf)$_3$

In a two-necked round-bottomed flask (100 mL) equipped with a reflux condenser, a solution of Ps-$AlCl_3$ (3 g, 8% DVB)[31] in freon 113 (50 mL) was prepared. To the stirred solution, 5 mL of triflic acid were added dropwise over a period of 2 h, while maintaining a gentle reflux. The mixture was then refluxed for 12 h. The polymer beads were filtered, washed with CH_2Cl_2 (50 mL) and then with Et_2O (50 mL), and dried in a vacuum oven overnight to give Ps-Al(OTf)$_3$ (3.41 g).

Typical Procedure for the Preparation of Acylals

Ps-Al(OTf)$_3$ (0.1 mmol) was added to a solution of 4-nitrobenzaldehyde (1 mmol) and Ac_2O (1.5 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was stirred using a magnetic stirrer at room temperature. Progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst was filtered off and washed with CH_2Cl_2 (15 mL). The filtrate was washed with water (10 mL), and then the organic layer was dried over anhydrous sodium sulfate and concentrated on a rotary evaporator under reduced pressure to give the desired pure product: Yield (94%), mp 125 °C (lit.[14] 124 °C); IR (KBr): 2948, 1755, 1620, 1530, 1359, 1242, 1210, 999 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.4$ (d, $J = 7.9$ Hz, 2H), 7.7 (d, $J = 7.9$ Hz, 2H), 7.5 (s, 1H), 2.1 (s, 6H). After each reaction, the spent polymeric catalyst from different experiments was washed with Et_2O, dried overnight in a vacuum oven, and reused.

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