

Polystyrene Supported Al(OTf)₃: an Environmentally Friendly Heterogeneous Catalyst for Friedel-Crafts Acylation of Aromatic Compounds

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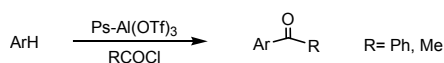
Stable and non-hygroscopic polystyrene supported aluminium triflate (Ps-Al(OTf)₃), which is prepared easily from cheap and commercially available compounds was found to be an environmentally friendly heterogeneous catalyst for Friedel-Crafts acylation of arenes using acid chlorides in the absence of solvent under mild reaction conditions. The catalyst can be reused up to five times after simple washing with dichloromethane.

Key Words: Acylation, Ketones, Heterogeneous catalysis, Aluminium triflate, Polystyrene

Introduction

Friedel-Crafts acylation of aromatic compounds is fundamental and important reaction in the production of aromatic ketones largely used as intermediates in the synthesis of pharmaceuticals, naproxen, dextromethorphan, dyes, and agrochemicals.^{1,2} Friedel-Crafts acylation involves electrophilic substitution of an aromatic compound with an acylating reagent in the presence of protic acids or Lewis acids as catalysts.³⁻²¹ The disadvantages associated with the classical procedures include a need for the use of stoichiometric or excess amounts of catalyst in reactions (due to consumption of the catalyst by complexation to starting materials and/or products), the use of unrecyclable catalysts which eventually result in generation of a large amount of environmentally hazardous waste materials, less selectivity of *para/ortho* isomers, tedious work-up, and the use of moisture-sensitive, expensive, hazardous or difficult to handle catalysts. Furthermore, in most of these methods applicable substrate range is very limited. Thus, a reliable general method for this useful reaction involving non-hazardous reagents is in demand.

In recent years, the use of solid supported catalysts has received considerable attention in different areas of organic synthesis due to their environmental compatibility, moisture and air tolerance, non-toxicity, non-corrosiveness, easier handling, and their reusability and the development of solvent-less protocol has an added advantage in the green context. In this pursuit, we found that Ps-Al(OTf)₃ was a good catalyst for highly chemoselective dithioacetalization of carbonyl compounds²² and the sulfonylation of arenes.²³ Along this line, we now wish to report that Ps-Al(OTf)₃ is also highly chemoselective catalyst for the acylation of aromatic compounds with acid chlorides in solvent-free conditions (Scheme 1).



Scheme 1

Experimental

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. Capacity of the catalyst was determined by Gravimetric method and atomic absorption technique using a Philips atomic absorption instrument. Reaction monitoring and purity determination of the products were accomplished by GLC or TLC on silica-gel polygram SILG/UV₂₅₄ plates. Gas chromatography was performed in an apparatus from Shimadzu. IR spectra were run on a Shimadzu model 8300 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker Advance DPX-300 spectrometer.

Preparation of Ps-Al(OTf)₃. This catalyst was prepared as reported in the literature.²² The loading of Al(OTf)₃ determined was 0.41 mmol/gr.

Typical experimental procedure. Anisole (5 mmol), benzoyl chloride (4 mmol), and Ps-Al(OTf)₃ (0.4 mmol) were combined and the reaction mixture was stirred magnetically at room temperature. After completion of the reaction (monitored by TLC), the catalyst was filtered off and washed with CH₂Cl₂. The filtrate was washed with aqueous solution of sodium bicarbonate and water and the organic layer was dried (Na₂SO₄) and concentrated on a rotary evaporator under reduced pressure to give the corresponding ketone. Whenever required, the products were purified by column chromatography (silica gel) using petroleum ether-ethyl acetate as eluent so as to afford the pure ketone.

Results and Discussion

Ps-Al(OTf)₃ was prepared by the exchange reaction between cross-linked polystyrene supported AlCl₃ (Ps-AlCl₃) and triflic acid in Freon-113 under reflux conditions. By using this catalyst different structures of aromatic rings underwent acylation with benzoyl chloride and acetyl chloride as acylating agents at room temperature in solvent-free conditions (Table 1). The optimum molar ratio of Ps-Al(OTf)₃ to acid chloride was 0.1:1. A tremendous enhancement of *para* selectivity was observed in the acylation of the substituted benzenes (entries 1-12). Naphthalene, 2-methoxynaphthalene, and anthracene were converted to the corresponding ketones with high regioselectivity in high

Table 1. Acylation of arenes with acid chlorides catalyzed by Ps-Al(OTf)₃^a

Entry	Arene	Acid Chloride	Product	Time (h)	Yield (%) (<i>o:m:p</i>) ^b
1		PhCOCl		1.6	90 ⁷
2	"	MeCOCl		1.4	91 ⁷
3		PhCOCl		1.2	96(5:0:95) ¹⁹
4	"	MeCOCl		1.1	92(5:4:91) ⁷
5		PhCOCl		1	97(6:3:91) ¹⁹
6		PhCOCl		1	96(94:6) ^{c,7}
7	"	MeCOCl		0.9	94(96:6) ^{c,7}
8		PhCOCl		1.1	92 ¹⁹
9		PhCOCl		1.6	92(4:0:96) ^{d,7}
10		PhCOCl		1.1	89(6:0:94) ⁷
11		PhCOCl		2	89(5:0:95) ⁷
12	"	MeCOCl		1.9	90(6:4:90) ⁷
13		PhCOCl		1.8	90(6:94) ^{e,7}
14	"	MeCOCl		1.7	91(9:91) ^{e,7}
15		PhCOCl		1.6	90 ^{d,19}
16		PhCOCl		2.1	90 ^{d,19}
17	"	MeCOCl		1.9	89 ^{d,7}
18		PhCOCl		2	94 ^{9,24}
19		PhCOCl		2.1	95 ^{10,25}
20		PhCOCl		2	88 ^{10,26}
21		MeCOCl		3.4	90 ^{d,27,28}

^aAll reactions carried out at room temperature in the absence of solvent, unless otherwise indicated. The molar ratio of Ps-Al(OTf)₃:acid chloride is 0.1:1. ^bIsolated Yields. Isomer distribution based on ¹H-NMR spectroscopy and GC. All products are known compounds and were identified by comparison of their physical and spectral data with those of the authentic samples. ^cIsomer distribution of 3,4-dimethylphenyl isomer to 2,3-dimethylphenyl isomer. ^dThe reaction was performed in 1,2-dichloroethane. ^e α : β ratio. The reaction was performed in 1,2-dichloroethane.

Table 2. Intramolecular Friedel-Crafts acylation using Ps-Al(OTf)₃^a

Substrate	Product	Time (h)	Yield (%) ^b
		2.5	94

^aThe reaction was carried out at 80 °C in nitrobenzene. The molar ratio of Ps-Al(OTf)₃:substrate is 0.12:1. ^bIsolated Yield.

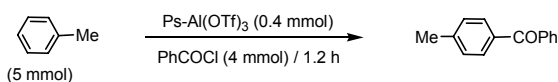
yields (entries 13-17). In the case of naphthalene the β -isomer was the major product (entries 13,14). The acylating agent is thought to be bulky Lewis acid-AcCl complex and hence attack at sterically more hindered α -position can't occur. This procedure is also good enough for the acylation of heterocyclic aromatic compounds such as furan, thiophene, and pyrrole, a conversion which is otherwise problematic in the presence of strong acid catalysts (entries 18-20). These reactions were regioselective, producing only the 2-acyl product in 88 - 95% yields. It was pleasing to observe that, indole was converted to its corresponding ketone with acetyl chloride in the presence of Ps-Al(OTf)₃ in 90% yield (entry 21). No *N*-substituted product was observed under these reaction conditions. Acylation of highly deactivated arenes such as nitrobenzene and 1,2-dichlorobenzene failed.

Following these results, we further investigated the potential of Ps-Al(OTf)₃ for the cyclization of 4-phenylbutanoic acid chloride. As it is shown in Table 2, 1-tetralone was produced in the presence of Ps-Al(OTf)₃ in 94% yield in nitrobenzene at 80 °C.

It is important to note that Ps-Al(OTf)₃ shows a higher catalytic activity than Ps-AlCl₃²⁹ and Al(OTf)₃³⁰ in acylation reactions. For example, the reaction of anisole with benzoyl chloride in the presence of excess amounts of Ps-AlCl₃ or Al(OTf)₃ after 3 h at room temperature produced *p*-methoxybenzophenone in 20 and 45% yields, respectively. Presumably, the less catalytic activity of Al(OTf)₃ than Ps-Al(OTf)₃ in acylation of arenes with acid chlorides is due to its ability to strongly complex Lewis base products. Unlike Al(OTf)₃, Ps-Al(OTf)₃ is a milder catalyst which forms no stable complex with starting materials and/or products.

When Ps-Al(OTf)₃ was used as a catalyst for acylation reactions, no band corresponding to -CO stretching in the IR spectrum of Ps-Al(OTf)₃ was observed after the reactions in either the presence or absence of substrate, indicating that polystyrene itself does not undergo acylation under experimental condition used. Probably acylation reactions are not favored with Ps-Al(OTf)₃ as a π complex is formed between polystyrene and Al(OTf)₃.

To find out whether the reaction takes place in the solid matrix of Ps-Al(OTf)₃ or whether Al(OTf)₃ simply released in the reaction medium is responsible for the acylation reaction, Ps-Al(OTf)₃ was added to benzene and the mixture was stirred at room temperature for 2 h. Then, the catalyst was filtered off and the filtrate was analyzed for its aluminium content, which showed a negligible release of Al(OTf)₃. The filtrate was found to be inactive for the acylation reaction. These observations



Use ^a	1	2	3	4	5
Yield (%)	96	95	95	93	91

^aRecovered catalyst was used successively (Use 2,3,...)

Scheme 2

Table 3. Comparison of the catalytic activity of Ps-Al(OTf)₃ against other reported catalysts for the acylation of anisole with benzoyl chloride

Catalyst	Solvent	Temp. (°C)	Time (h)	Yield (%) (o:p)
Ps-Al(OTf) ₃	neat	rt	1	97 (6:91)
Sc(OTf) ₃	CH ₃ NO ₂	50	18	79 ⁴
BiCl ₃	neat	110	6	96 ⁶
Zn powder	neat(MW)	120	10 (s)	71 ⁷
AlPW ₁₂ O ₄₀	neat	60 - 70	2	94 (20:80) ⁸
Al metal powder	neat	82(MW)	10	81 ¹¹
InCl ₃ -[C ₄ mim]Cl ^a	neat	100	18	94 (6:94) ¹²
SmI ₃	CH ₃ CN	45	4	61 ¹³
MoO ₂ Cl ₂	neat	reflux	20	85 (0:100) ²⁰

^aChloroindate(III) ionic liquid.

indicate that Ps-Al(OTf)₃ is stable under the reaction conditions and there is no leaching of acid moieties during reactions.

In order to know whether Ps-Al(OTf)₃ could be reused to catalyze the acylation reaction, a sample of the solid catalyst was recovered by filtration after the reaction and it was then reused in an identical reaction of anisole with benzoyl chloride. As it is shown in Scheme 2 the efficiency of the recycled catalyst did not change appreciably after five cycles.

A comparison of the present procedure, using Ps-Al(OTf)₃, with selected previously known protocols is collected in Table 3. As it is seen in addition to having the general advantages attributed to the solid supported catalysts, Ps-Al(OTf)₃ has a good efficiency compared to other recently reported catalysts.

Conclusion

In conclusion Ps-Al(OTf)₃ is an effective catalyst for the acylation of arenes with acid chlorides under modest conditions. The catalyst is stable (as a bench top catalyst) and can be recovered to reuse without regeneration, which renders the process economically attractive. Short reaction times, easy work-up, high to excellent yields, chemoselectivity, and easy preparation and handling of the catalyst are other obvious advantages of the present method. In addition, the use of Ps-Al(OTf)₃ has resulted in a reduction in the unwanted and hazardous waste that is produced during conventional homogeneous processes.

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