



Full paper/Mémoire

Polystyrene-supported GaCl_3 : A new, highly efficient and recyclable heterogeneous Lewis acid catalyst for acetylation and benzylation of alcohols and phenols

Ali Rahmatpour

Polymer Science and Technology Division, Research Institute of Petroleum Industry (RIPI), 14665-1137 Tehran, Iran

ARTICLE INFO

Article history:

Received 5 March 2012

Accepted after revision 13 August 2012

Available online 29 September 2012

Keywords:

Polymer- supported catalyst

Alcohol

Acetylation

Heterogeneous Lewis acid catalyst

Phenol

ABSTRACT

A new, simple and highly chemoselective method for both acetylation and benzylation of alcohols and phenols with acetic anhydride in the presence of polystyrene-supported gallium trichloride (PS/GaCl_3) as a highly active and reusable heterogeneous Lewis acid catalyst is presented. In this catalytic system, primary, secondary and tertiary alcohols as well as phenols were converted to the corresponding acetates and benzoates with high yields. The heterogenized catalyst is of high reusability and stability in the acetylation reactions and was recovered several times with negligible loss in its activity or a negligible catalyst leaching, and also there is no need for regeneration. Remarkably, a selective mono-acetylation of symmetrical diols can be achieved chemoselectively by employing the same catalyst.

© 2012 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.

1. Introduction

Conventional Lewis acids are very effective catalysts for a wide variety of organic reactions [1], but one of the major problems associated with these homogeneous catalysts is the recovery of catalyst from the reaction medium. In recent years, there have been intense efforts to develop methods recovering and reusing the homogeneous catalysts [2–6]. Immobilization of catalysts on a solid support improves the available active sites, stability, hygroscopic properties, handling, and reusability of catalysts which factors are important in industry [7]. Therefore, use of supported and reusable catalysts in organic transformations has economical and environmental benefits. A large number of polymer-supported Lewis acid catalysts have been prepared by immobilization of the catalysts on polymer via coordination or covalent bonds [8]. Such polymeric catalysts are usually as active and selective as their homogeneous or solution-phase counterparts while having the distinguishing characteristics of being easily

separable from the reaction mixture, recyclability, easier handling, non-toxicity, enhanced stability, and improved selectivity in various organic reactions. Polystyrene is one of the most widely studied heterogeneous and polymeric supports due to its environmental stability and hydrophobic nature which protects water-sensitive Lewis acids from hydrolysis by atmospheric moisture until it is suspended in an appropriate solvent where it can be used in a chemical reaction [4]. It is well known that gallium trichloride is a strong Lewis acid and an important catalyst in organic transformations. However, it easily hydrolyzes in air, so that its use, storage, and separation from the reaction mixture are inconvenient and difficult. Polystyrene-supported gallium chloride, PS/GaCl_3 , which is a tightly bound and stable complex between anhydrous GaCl_3 and polystyrene-divinylbenzene copolymer beads, has been described for the first time by Ruicheng et al. [9]. The use of PS/GaCl_3 complex catalyst has several advantages over conventional Lewis acid catalyst such as its cost-effectiveness, ease of handling, recyclability, and tunable Lewis acidity.

Acylation of alcohols and phenols is of enormous interest in organic synthesis as it provides a useful and

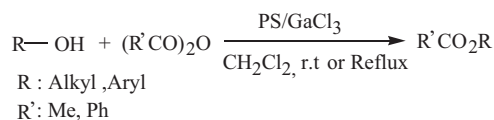
Email address: rahmatpoura@ripi.ir.

efficient protection protocol in a multistep synthetic process [10]. Moreover, this reaction has biological significance because of the presence of alcoholic and phenolic hydroxyl groups in a variety of biologically active compounds that necessitates the manipulation of the chemical reactivity of these functional groups during the synthesis of multifunctional synthetic targets possessing one or more of these groups. Acylation is usually carried out by treatment of an alcohol or phenol with acetyl chloride or acetic anhydride in the presence of an acid or a base catalyst in a suitable organic solvent, although acetic anhydride is the most commonly used, as it is less toxic. However, the catalysts traditionally used are bases or acids, which have many disadvantages in the acetylation process. For example, some of the base catalysts are toxic, flammable, and possess offensive odors [11,12]. In addition, some of the traditional protic acid catalysts are not entirely satisfactory in terms of the stability of reactants or products under the reaction conditions and the time-consuming work-up procedures. A variety of procedures using homogeneous or heterogeneous catalysts such as *p*-TSA [13], CoCl_2 [14], alumina [15], montmorillonite K-10 and KSF [16], zeolite HSZ-360 [17], MgBr_2 [18], $\text{Bi}(\text{TFA})_3$ [19], TaCl_5 [20], $\text{NH}_2\text{SO}_3\text{H}$ [21], $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ [22], 3-nitrobenzene boronic acid [23], TMSOTf [24], $\text{Cp}_2\text{Ti}(\text{O}-\text{SO}_2\text{C}_8\text{F}_{17})_2$ [25], Cp_2ZrCl_2 [26], $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ [27], $\text{Mg}(\text{ClO}_4)_2$ [28], $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ [29], $\text{HBF}_4 \cdot \text{SiO}_2$ [30], $\text{Cu}(\text{BF}_4)_2$ [31], $\text{HClO}_4 \cdot \text{SiO}_2$ [32], electron-deficient tin (IV) porphyrins [33–35], alumina-supported MoO_3 [36], zirconium sulfophenyl phosphonate [37], *o*-benzene disulfonimide [38], saccharinsulfonic acid [39], cerium polyoxometallate [40], $\text{BiO}(\text{ClO}_4)_2$ [41], cobalt(II) and Mn(III) salen complexes [42], $\text{Gd}(\text{OTf})_3$ [43], InCl_3 [44], $\text{Ph}_3\text{P}^+\text{CH}_2\text{COCH}_3\text{Br}^-$ [45], $[\text{Mn}(\text{III})-(\text{haacac})\text{Cl}]$ complex [46], and LiOTf [47] have been reported for acetylation of alcohols and phenols with acetic anhydride. However, most of the catalysts suffer from limitations such as long reaction times, harsh reaction condition or tedious work-up, use of expensive, moisture sensitive and toxic catalysts, regulatory constraints, the occurrence of side reactions, intolerance to other functional groups, poor selectivity, and high catalyst to substrate ratio. Apart from these difficulties, most above methods do not satisfy the requirements of green synthesis due to the inability to recovery and reuse of the catalyst. As a result, new kinds of catalysts, especially using recyclable heterogeneous catalysts or mild, selective and environmentally benign methodologies for these transformations are still in demand.

In continuation of our recent works on the use of polymeric Lewis acid catalysts in organic transformations [48,49], herein we report the preparation and investigation of catalytic activity of polystyrene-supported gallium chloride as a stable, highly active and reusable heterogeneous catalyst in the acetylation and benzylation of alcohols and phenols with acetic and benzoic anhydride, (Ac_2O), (PhCO_2O), respectively (Scheme 1).

2. Experimental

All chemical reagents were obtained from Fluka or Merck chemical companies and were used without further purification. Cross-linked polystyrene (5–7% divinylbenzene, mesh size: 20–75 mm) was prepared via suspension



Scheme 1. Acetylation and benzylation of alcohols and phenols with Ac_2O and (PhCO_2O) catalyzed by PS/GaCl₃.

polymerization as reported in the literature [48]. PS/AlCl₃ was also prepared as previously reported [49]. ¹H and ¹³C NMR spectra were recorded on a Bruker DPX-250 Avance spectrometer at 250.13 MHz. FT-IR spectra of the samples were recorded from 400 to 4000 cm⁻¹ on a Unicam Matteson 1000 spectrophotometer. UV spectra were taken using a Pharmacia Biotech Ultraspec 3000 model 80-2106-20 spectrometer. Gas chromatography experiments (GC) were performed with a Shimadzu GC-16A instrument using a 2 m column packed with silicon DC-200 or Carbowax 20 M. The capacity of the catalyst was determined by the gravimetric method (Mohr titration method) and atomic absorption technique using a Philips atomic absorption instrument. Reaction monitoring and purity determination of the products were accomplished by TLC on silica gel polygram SILG/UV₂₅₄ plates.

2.1. Preparation of polystyrene-supported gallium trichloride (PS/GaCl₃)

Anhydrous GaCl₃ (4 g) was added to polystyrene (8% divinylbenzene, mesh size: 20–75 mm, 8 g) in carbon disulfide (30 mL) as the reaction medium. The mixture was stirred using a magnetic stirrer under reflux condition for 1 h, cooled, and then water (50 mL) was cautiously added to hydrolyze the excess GaCl₃. The mixture was stirred until the bright red color disappeared, and the polymer became yellow. The polymer beads were collected by filtration and washed with water (300 mL) and then with ether (30 mL) and chloroform (30 mL). The catalyst was dried in a vacuum oven overnight at 50 °C before use. The chlorine content of PS/AlCl₃ was 4.17% analyzed by the Mohr titration method [50] and the loading capacity of GaCl₃ on the polymeric catalyst or the amount of GaCl₃ complexed with polystyrene was calculated to be 0.391 mmol/g.

2.2. General experimental procedure for acetylation of alcohols and phenols with Ac_2O catalyzed by PS/GaCl₃ complex

To a solution of alcohol or phenol (1 mmol) and Ac_2O (1.1–1.3 mmol) in methylene chloride (5 mL) was added PS/GaCl₃ (0.1 mmol) and the resulting mixture was stirred at room temperature. The progress of the reaction was monitored by TLC and GLC. After completion of the reaction, the catalyst was filtered off and washed with methylene chloride (2 × 10 mL) and the filtrate concentrated on a rotary evaporator under reduced pressure to afford the crude acetate product. Further purification was achieved by column chromatography on silica gel (Merck, 100–200 mesh, hexane-EtOAc, 90/10, v/v). The spent polymeric catalyst from different experiments was

combined, washed with ether and dried overnight in a vacuum oven and reused.

2.3. General experimental procedure for benzylation of alcohols and phenols with $(\text{PhCO})_2\text{O}$ catalyzed by PS/GaCl₃ complex

To a solution of alcohol or phenol (1 mmol) and $(\text{PhCO})_2\text{O}$ (1.2–1.5 mmol) in methylene chloride (10 mL) was added PS/GaCl₃ (0.1 mmol) and the resulting mixture was stirred under reflux conditions for the appropriate time according to Table 2. The progress of the reaction followed by GLC or TLC. After completion of the reaction, the catalyst was filtered off and washed with methylene chloride (2 × 10 mL) and the filtrate concentrated on a rotary evaporator under reduced pressure to afford the crude benzoate product which was passed through a short pad of silica gel (Merck, 100–200 mesh, hexane-EtOAc, 95/5, v/v) to provide the pure benzyolated product.

2.4. Catalyst recovery and reuse

The reusability of the catalyst was checked in the multiple acetylation of benzyl alcohol. At the end of each reaction, the solvent was evaporated, ether (Et₂O, 10 mL) was added and the catalyst was filtered. The recovered catalyst was used with fresh benzyl alcohol, Ac₂O and CH₂Cl₂.

3. Results and discussion

3.1. Preparation of PS/GaCl₃ complex

First, cross-linked polystyrene (5–7% divinylbenzene, mesh size: 20–75 mm) was prepared via suspension polymerization as reported in the literature [48]. Then, PS/GaCl₃ was prepared by addition of anhydrous gallium chloride to polystyrene (8% divinylbenzene) in carbon disulfide under reflux conditions. The loading capacity of the polymeric catalyst obtained by gravimetric method and checked by atomic absorption technique was 0.391 mmol GaCl₃/g of complex beads catalyst [50]. The data obtained by these two techniques showed, within experimental error, that the catalyzing species are in the form of GaCl₃ supported on the polymeric support. The UV spectrum of the solution of PS-GaCl₃ complex in CS₂ showed a new strong band at 470 nm, which is due to the formation of a stable $\pi \rightarrow p$ type coordination complex between the benzene rings in the polystyrene carrier with gallium trichloride. The FT IR spectrum of PS/GaCl₃ showed new absorption peaks due to the C–C stretching vibration and the C–H bending vibration of the benzene ring at 1500 to 1560 and 400 to 800 cm⁻¹, by which complex formation was demonstrated. The structure of the PS-GaCl₃ complex is similar to that of the PS-AlCl₃ complex as suggested by Neckers et al. [51], because the Lewis acid GaCl₃ is complexed with the benzene rings of the polystyrene and the GaCl₃ is stabilized due to the decreased mobility of the benzene rings hindered by the long polystyrene chain. The PS-GaCl₃ complex catalyst is a non-hygroscopic, water-tolerant, and especially stable species. In addition, this

polymeric catalyst is easy to prepare, stable in air for a long time (over 2 years) without any change, easily recycled and reused without appreciable loss of its activity.

3.2. Acetylation and benzylation of alcohols and phenols with Ac₂O and $(\text{PhCO})_2\text{O}$ catalyzed by PS/GaCl₃

In our initial evaluations, we used as the model reaction, the reaction of benzyl alcohol (1 equiv.) with acetic anhydride (1.1 equiv.). The choice of the solvent appeared crucial in order to maximize yield. Among the various solvents surveyed, the highest yield was obtained in CH₂Cl₂ (Table 1, entry 7). The highest yield obtained by using CH₂Cl₂ as the solvent can be ascribed to the fruitful swelling of the polymer network of the catalyst in this media, allowing the metal particles located inside the polymer matrix to effect the catalysis. The optimum molar ratio of the polymeric catalyst to hydroxyl compound was found to be 0.1:1. The key role played by the Lewis acidity of the heterogeneous catalyst PS/GaCl₃ was proved by employing the polystyrene beads (Table 1, entry 9) and the GaCl₃-benzene complex as catalysts. In fact, while in the former case no reaction occurred, which indicated that polystyrene itself did not promote the reaction, in the latter, the desired product was isolated in low yield 46% (Table 1, entry 10). Also, PS/GaCl₃ was found to be a more effective catalyst than PS/AlCl₃ in terms of reaction time and the yield of the product for acetylation of benzyl alcohol under identical conditions (Table 1, entry 12). We then turned our attention on whether the same catalyst could be employed for acetylation of alcohols using acetic acid and ethyl acetate as acylating agents. For this purpose, the model reaction was carried out with acetic acid and ethyl acetate under identical conditions, and only 36% and 23% of the corresponding acetates were produced, respectively.

When using a heterogeneous and metal-supported catalyst one of the most important issues is the possibility

Table 1
Reaction conditions optimization in the acetylation of benzyl alcohol with Ac₂O catalyzed by PS/GaCl₃ at room temperature.^a

Entry	Solvent	Catalyst (mol %)	Time (min)	Yield ^b (%)
1	n-Hexane	10	25	17
2	THF	10	25	21
3	CH ₃ Cl	10	25	40
4	CH ₃ CN	10	25	58
5 ^c	CH ₂ Cl ₂	–	60	NR
6	CH ₂ Cl ₂	5	25	60
7	CH ₂ Cl ₂	10	25	97
8	CH ₂ Cl ₂	20	25	97
9 ^d	CH ₂ Cl ₂	–	25	NR
10 ^e	CH ₂ Cl ₂	–	25	46
11 ^f	CH ₂ Cl ₂	10	15	NR
12 ^g	CH ₂ Cl ₂	10	60	76

NR: no reaction.

^a Reaction conditions: benzyl alcohol (1 mmol), Ac₂O (1.1 mmol), solvent (5 mL).

^b Isolated yield.

^c No catalyst.

^d PS was used as catalyst.

^e The toluene-GaCl₃ complex was used as catalyst.

^f Catalyst was filtered after 15 min.

^g PS/AlCl₃ was used as catalyst.

Table 2
Acetylation^a and benzylation^b of alcohols and phenols with Ac₂O and (PhCO)₂O catalyzed by PS/GaCl₃.





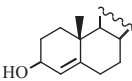
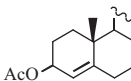
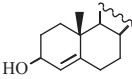
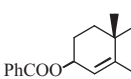




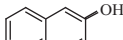
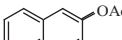
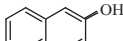
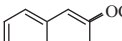
Entry	Substrate	Ratio ^c	Product ^d	Time (min)	Yield ^e (%)
1	C ₆ H ₅ CH ₂ OH	1:1.1	C ₆ H ₅ CH ₂ OAc	25	97
	C ₆ H ₅ CH ₂ OH	1:1.2	C ₆ H ₅ CH ₂ OCOPh	45	90
2	<i>p</i> -(Cl)C ₆ H ₄ CH ₂ OH	1:1.1	<i>p</i> -(Cl)C ₆ H ₄ CH ₂ OAc	30	93
	<i>p</i> -(Cl)C ₆ H ₄ CH ₂ OH	1:1.2	<i>p</i> -(Cl)C ₆ H ₄ CH ₂ OCOPh	50	89
3	<i>p</i> -(NO ₂)C ₆ H ₄ CH ₂ OH	1:1.1	<i>p</i> -(NO ₂)C ₆ H ₄ CH ₂ OAc	30	91
	<i>p</i> -(NO ₂)C ₆ H ₄ CH ₂ OH	1:1.2	<i>p</i> -(NO ₂)C ₆ H ₄ CH ₂ OCOPh	65	88
4	<i>o</i> -(NO ₂)C ₆ H ₄ CH ₂ OH	1:1.1	<i>o</i> -(NO ₂)C ₆ H ₄ CH ₂ OAc	70	91
	<i>o</i> -(NO ₂)C ₆ H ₄ CH ₂ OH	1:1.2	<i>o</i> -(NO ₂)C ₆ H ₄ CH ₂ OCOPh	100	84
5	<i>p</i> -(CH ₃)C ₆ H ₄ CH ₂ OH	1:1.1	<i>p</i> -(CH ₃)C ₆ H ₄ CH ₂ OAc	28	96
	<i>p</i> -(CH ₃)C ₆ H ₄ CH ₂ OH	1:1.2	<i>p</i> -(CH ₃)C ₆ H ₄ CH ₂ OCOPh	45	89
6	<i>p</i> -(OCH ₃)C ₆ H ₄ CH ₂ OH	1:1.1	<i>p</i> -(OCH ₃)C ₆ H ₄ CH ₂ OAc	27	94
	<i>p</i> -(OCH ₃)C ₆ H ₄ CH ₂ OH	1:1.2	<i>p</i> -(OCH ₃)C ₆ H ₄ CH ₂ OCOPh	50	90
7	<i>n</i> -CH ₃ (CH ₂) ₆ CH ₂ OH	1:1.1	<i>n</i> -CH ₃ (CH ₂) ₆ CH ₂ OAc	40	95
	<i>n</i> -CH ₃ (CH ₂) ₆ CH ₂ OH	1:1.2	<i>n</i> -CH ₃ (CH ₂) ₆ CH ₂ OCOPh	55	89
8	<i>n</i> -CH ₃ (CH ₂) ₅ CH ₂ OH	1:1.1	<i>n</i> -CH ₃ (CH ₂) ₅ CH ₂ OAc	40	94
	<i>n</i> -CH ₃ (CH ₂) ₅ CH ₂ OH	1:1.2	<i>n</i> -CH ₃ (CH ₂) ₅ CH ₂ OCOPh	55	88
9	CH ₃ (CH ₂) ₃ CH(OH)CH ₃	1:1.1	CH ₃ (CH ₂) ₃ CH(OAc)CH ₃	40	93
	CH ₃ (CH ₂) ₃ CH(OH)CH ₃	1:1.2	CH ₃ (CH ₂) ₃ CH(OCOPh)CH ₃	50	86
10	(CH ₃) ₂ CHOH	1:1.1	(CH ₃) ₂ CHOAc	40	92
	(CH ₃) ₂ CHOH	1:1.2	(CH ₃) ₂ CHOCOPh	50	87
11	C ₆ H ₅ CH(CH ₃)CH ₂ OH	1:1.1	C ₆ H ₅ CH(CH ₃)CH ₂ OAc	55	92
	C ₆ H ₅ CH(CH ₃)CH ₂ OH	1:1.2	C ₆ H ₅ CH(CH ₃)CH ₂ OCOPh	75	88
12	C ₆ H ₅ CH(CH ₃)OH	1:1.2	C ₆ H ₅ CH(CH ₃)OAc	55	94
	C ₆ H ₅ CH(CH ₃)OH	1:1.2	C ₆ H ₅ CH(CH ₃)OCOPh	80	85
13	C ₆ H ₅ C(CH ₃) ₂ OH	1:1.3	C ₆ H ₅ C(CH ₃) ₂ OAc	70	94
	C ₆ H ₅ C(CH ₃) ₂ OH	1:1.4	C ₆ H ₅ C(CH ₃) ₂ OCOPh	90	86
14		1:1.2		65	92
		1:1.3		85	87
15	CH ₂ =CHCH ₂ OH	1:1.2	CH ₂ =CHCH ₂ OAc	90	90
	CH ₂ =CHCH ₂ OH	1:1.3	CH ₂ =CHCH ₂ OCOPh	90	86
16		1:1.3		90	92
		1:1.5		100	83
17	C ₆ H ₅ OH	1:1.3	C ₆ H ₅ OAc	50	94
	C ₆ H ₅ OH	1:1.4	C ₆ H ₅ OCOPh	80	86
18	<i>p</i> -(OCH ₃)C ₆ H ₄ OH	1:1.2	<i>p</i> -(OCH ₃)C ₆ H ₄ OAc	45	94
	<i>p</i> -(OCH ₃)C ₆ H ₄ OH	1:1.3	<i>p</i> -(OCH ₃)C ₆ H ₄ OCOPh	50	89
19	<i>p</i> -(CH ₃)C ₆ H ₄ OH	1:1.2	<i>p</i> -(CH ₃)C ₆ H ₄ OAc	45	93
	<i>p</i> -(CH ₃)C ₆ H ₄ OH	1:1.3	<i>p</i> -(CH ₃)C ₆ H ₄ OCOPh	50	88
20	<i>p</i> -(CHO)C ₆ H ₄ OH	1:1.2	<i>p</i> -(CHO)C ₆ H ₄ OAc	65	91
	<i>p</i> -(CHO)C ₆ H ₄ OH	1:1.3	<i>p</i> -(CHO)C ₆ H ₄ OCOPh	120	82
21		1:1.3		70	91
		1:1.4		100	82

Table 2 (Continued)

Entry	Substrate	Ratio ^c	Product ^d	Time (min)	Yield ^e (%)
22		1:1.3		70	92
		1:1.4		100	81
23	HOCH ₂ (CH ₂) ₃ CH ₂ OAc	1:1.1	AcOCH ₂ (CH ₂) ₃ CH ₂ OAc	45	92
24	HOCH ₂ (CH ₂) ₆ CH ₂ OBn	1:1.1	AcOCH ₂ (CH ₂) ₆ CH ₂ OBn	40	92
25	HOCH ₂ (CH ₂) ₆ CH ₂ OBz	1:1.1	AcOCH ₂ (CH ₂) ₆ CH ₂ OBz	40	92
26	HOCH ₂ (CH ₂) ₃ CH ₂ OTs	1:1.1	AcOCH ₂ (CH ₂) ₃ CH ₂ OTs	45	91

^a All acetylation reactions were carried out in CH₂Cl₂ (5 mL) in the presence of PS/GaCl₃ (0.1 mmol) at room temperature.

^b All benzoylation reactions were carried out in refluxing CH₂Cl₂ (5 mL) in the presence of PS/GaCl₃ (0.1 mmol).

^c The mole ratio of (substrate/Ac₂O and substrate/(PhCO)₂O).

^d All the acetate and benzoate products were identified by comparison of their physical and spectral data with those of authentic samples.

^e Isolated yield.

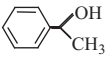
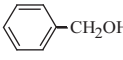
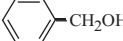

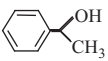
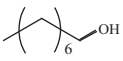
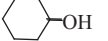

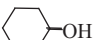
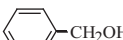

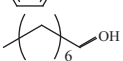
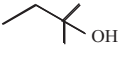

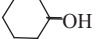

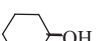
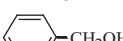
of leaching of the reactive center into the reaction mixture, particularly for practical applications of the reaction. Our preliminary investigations demonstrated that PS/GaCl₃ catalyst (a stable π complex) is very stable to air and moisture. To rule out the contribution of concurrent homogeneous catalysis in the results shown in Table 2, the catalyst was allowed to react with dry methylene chloride for 15 min under the operated reaction conditions and then filtered off. We observed that the filtrate (the catalyst-free liquid) showed no catalytic activity in acetylation of benzyl alcohol under the operated reaction condition (Table 1, entry 11). On the other hand, after each run, the filtrates were used for determination of catalyst leaching (gallium content), which showed a negligible release of GaCl₃ by atomic absorption spectroscopy or ICP measurement. The

capacity of the catalyst after six uses was 0.38 mmol of GaCl₃ per gram. Also, the catalytic behavior of the separated liquid was tested by addition of fresh benzyl alcohol and Ac₂O to the filtrates after each run. Execution of the acetylation reaction under the same reaction conditions, as with catalyst, showed that the obtained results were as same as blank experiments. These findings confirmed that PS/GaCl₃ is stable and no significant leaching of Lewis acid moieties is operating under our reaction conditions and that the observed catalysis is truly heterogeneous in nature.

Further, we carried out the reactions between Ac₂O and various alcohols to explore the reaction scope of PS/GaCl₃-catalyzed acetylation, the results are summarized in Table 2. As can be seen, all reactions proceeded very cleanly

Table 3

Selective acetylation^a and benzoylation^b of alcohols and phenols catalyzed by PS/GaCl₃.

Entry	Subst. 1	Subst. 2	Subst. 1/Subst. 2/(Ac ₂ O) or (PhCO) ₂ O	Time (min)	Yield (%) ^c	
					Ester 1	Ester 2
1			1:1.1	50	3	93
2			1:1:1.1 (1.2) ^d	50 (75) ^e	4 (7) ^f	94 (91) ^f
3			1:1:1.1 (1.2)	50 (85)	4 (8)	93 (90)
4			1:1:1.1 (1.2)	65	5	92
5			1:1:1.1 (1.2)	60 (85)	4 (8)	92 (89)
6			1:1:1.1	55	3	93
7			1:1:1.1	90	4	92
8			1:1:1.2 (1.4)	85 (100)	4 (9)	92 (87)
9			1:1:1.2 (1.4)	60 (85)	3 (6)	94 (90)

^a All acetylation reactions were carried out in CH₂Cl₂ (5 mL) in the presence of PS/GaCl₃ (0.1 mmol) at room temperature.

^b All benzoylation reactions were carried out in refluxing CH₂Cl₂ (10 mL) in the presence of PS/GaCl₃ (0.1 mmol).

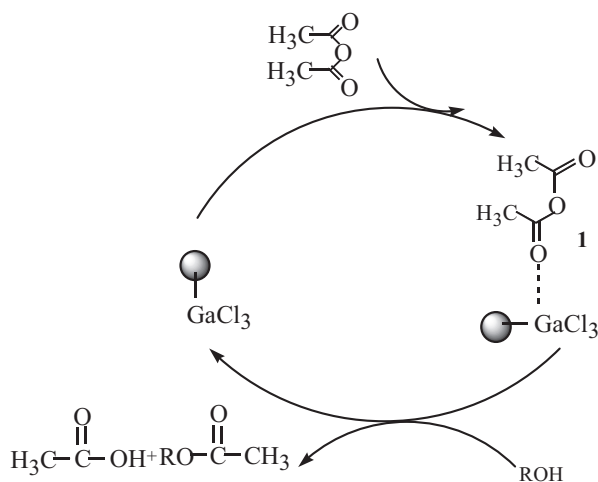
^c Yields based on GC and NMR.

^{d, e, f} The molar ratios, times and yields in the parentheses refer to benzoylation reactions.

(checked by GC) in good to excellent yields. A broad selection of alcohols, including primary (benzylic and linear ones), secondary (including aliphatic and aromatic alcohols), tertiary and allylic alcohols, were converted to their corresponding acetates successfully at room temperature (Table 2). It is noteworthy that in the case of both tertiary and allylic alcohols, which are acid-sensitive alcohols, no elimination product or migration of C=C bonds (rearrangement) was observed when PS/GaCl₃ was used, probably due to its mild catalytic activity and they were also converted to their corresponding acetates in high yields (Table 2, entries 13, 15, 16). Protection of phenolic hydroxyl group was also achieved under the same reaction conditions described for alcohols and the corresponding acetates were produced in high yields (Table 2). As can be seen, a phenol whose benzene ring substituted with a strong electron-donating group, reacted quickly with excellent yield (Table 2, entries 18, 19). We then turned our attention on whether the same catalyst could be useful for acetylation of substrates containing other protecting groups. We observed that various protected alcohols (Table 2, entries 23–26) containing protecting groups such as acetyl, benzyl, benzoyl and tosyl were smoothly converted into the corresponding acetates without affecting the other protecting groups.

In order to extend the scope of the catalyst further, the benzylation of alcohols and phenols with benzoic anhydride, a less reactive anhydride, was also investigated. The results of this investigation are shown in Table 2. Treatment of a series of alcohols and phenols with benzoic anhydride in the presence catalytic amount of PS/GaCl₃ provided the corresponding benzoates in good yields (Table 2, entries 1–22).

In order to show that whether the presented method is potentially applicable for chemoselective conversion of alcohols and phenols to the corresponding acetates or benzoates, a set of competitive reactions was allowed between a primary alcohols and a secondary or tertiary alcohols, or phenol with Ac₂O and (PhCO)₂O in the presence of PS/GaCl₃ (Table 3). The results indicated that PS/GaCl₃ was able to discriminate between different types



Scheme 2. The proposed catalytic mechanism for the formation of acetates.

of alcohols and or phenols from each other, a transformation that is difficult to accomplish via conventional methods (Table 3, entries 1–9).

The definite mechanism of the reaction is unclear. However, a plausible mechanism for the formation of acetates in the presence of PS/GaCl₃ as a catalyst is shown in Scheme 2. The acetic anhydride is first activated by Ga(III) as a Lewis acid to afford **1**. The hydroxyl compound attacks **1** which in turn converts to the final product and simultaneously releases the catalyst for the next catalytic cycle.

In order to show the efficiency and applicability of the present method, the catalytic activity of PS/GaCl₃ was compared with that of some reported catalysts in the literature, the results are summarized in Table 4. The results have been compared with respect to the reaction times, mol-% of the catalyst used, and yields. As demonstrated in Table 4, PS/GaCl₃ is an equally or more efficient catalyst for this acetylation reaction in terms of yield and reaction rate.

Table 4

Comparison of the results obtained for the acetylation of benzyl alcohol catalyzed by PS/GaCl₃ with those obtained by some reported catalysts.

Entry	Catalyst (mol %)	Conditions	Time (min)	Yield (%)	Ref.
1	BiCl ₃ (10)	CH ₃ CN, reflux	35	98	[19]
2	Bi(TFA) ₃ (5)	CH ₃ CN, reflux	60	96	[19]
3	CoCl ₂ (0.5)	CH ₃ CN, RT	240	98	[14]
4	Montmorillonite KSF (20 mg)	Solvent-free, RT	60	90	[16]
5	ZeoliteHSZ-360 (20 mg)	Solvent-free, 60 °C	60	84	[17]
6	Saccharinsulfonic acid (13 mg)	CH ₂ Cl ₂ /reflux	120	90	[39]
7	Gd(OTf) ₃ (0.1)	CH ₃ CN, RT	30	97	[43]
8	Cobalt(II) salen complex (1)	Solvent-free, 50 °C	45	99	[42]
9	Cu(BF ₄) ₂ .XH ₂ O	Solvent-free, RT	60	96	[31]
10	Cp ₂ ZrCl ₂ (1)	Solvent-free, RT	10 h	93	[26]
11	TaCl ₅ (10)	CH ₂ Cl ₂ , RT	120	96	[20]
12	Mn(III) salen complex (7)	Toluene, 80 °C	6 h	93	[42]
13	HBF ₄ -SiO ₂ (1)	Solvent-free, RT	60	94	[30]
14	InCl ₃ (0.1)	Solvent-free, RT	30	85	[44]
15	Ph ₃ P ⁺ CH ₂ COCH ₃ Br ⁻ (5)	Solvent-free, RT	35	96	[45]
16	[Mn(III)(haacac)Cl] complex	CH ₃ NO ₂ , RT	5 h	97	[46]
17	LiOTf (20)	Solvent-free, RT	12 h	97	[47]
18	PS/GaCl ₃ (10)	CH ₂ Cl ₂ , RT	25	97	Table 2

Table 5Reusability of ^aPS/GaCl₃ in the acetylation of benzyl alcohol with Ac₂O.^b

Run	Benzyl acetate (%) ^c	Time (min)
1	97	25
2	97	25
3	96	25
4	96	25
5	95	25
6	94	25

^a The capacity of the catalyst after six uses was 0.38 mmol GaCl₃ per gram.^b Reaction conditions: benzyl alcohol (1 mmol), Ac₂O (1.1 mmol), PS/GaCl₃ (0.1 mmol), CH₂Cl₂ (5 mL)^c Isolated yield.

3.3. Catalyst reusability

Finally, the reusability of the catalyst was tested in the acetylation reaction of benzyl alcohol with acetic anhydride as a model substrate. For each of the repeated reactions, the catalyst was filtered, washed exhaustively with methylene chloride and diethyl ether, respectively, and dried before using with fresh benzyl alcohol and Ac₂O. The catalyst was consecutively reused six times with negligible loss in its activity or a negligible catalyst leaching, and also there is no need for regeneration (Table 5).

4. Conclusion

In conclusion, in this article a simple, mild, efficient and highly chemoselective method for both acetylation and benzylation of alcohols and phenols using stable and heterogeneous polystyrene-supported gallium trichloride is reported. The short reaction times, high to excellent yields, low cost, easy preparation and handling of the polymeric Lewis acid catalyst are the advantages of the present method. In addition, the use of water-tolerant PS/GaCl₃ has resulted in a reduction in the unwanted and hazardous waste and minimum amount of product contamination with metal that is produced during conventional homogeneous processes. Most importantly, the work-up is reduced to a mere filtration and evaporation of the solvent. Finally, this catalytic system showed a good catalytic activity in these reactions and this polymeric catalyst can be recovered unchanged and used again at least six times with negligible loss in its activity. The other applications of PS/GaCl₃ is currently under investigation and will be reported in due course.

References

- [1] H. Yamamoto (Ed.), *Lewis Acids in Organic Synthesis*, Wiley-VCH, Weinheim, 2002.
- [2] S.V. Ley, I.R. Baxendale, R.N. Bream, P.S. Jackson, A.G. Leach, D.A. Longbottom, M. Nesi, J.S. Scott, R.I. Storer, S.J. Taylor, *J. Chem. Soc. Perkin Trans. 1* (23) (2000) 3815.
- [3] D.C. Bailey, S.H. Langer, *Chem. Rev.* 81 (1981) 109.
- [4] A. Akela, A. Moet, *Functionalized Polymers and Their Applications*, Wiley, New York, 1990, p. 11.
- [5] N.E. Leadbeater, M. Marco, *Chem. Rev.* 102 (2002) 3217.
- [6] A. Akela, *Chem. Rev.* 81 (1981) 557.
- [7] J.H. Clarck, *Catalysis of Organic reactions by Supported Inorganic Reagents*, VCH, Weinheim, 1994, p. 126.
- [8] K. Smith, *Solid Supports and Catalysts in Organic Synthesis*, Ellis Horwood, Chichester, 1992.
- [9] R. Ruicheng, J. Shuojian, S. Ji, *J. Macromol. Sci. Chem. A* 24 (6) (1987) 669.
- [10] T.W. Greene, P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., John Wiley & Sons, New York, 2000.
- [11] G. Hofle, W. Steglich, H. Vorbruggen, *Angew. Chem. Int. Ed.* 17 (1978) 569.
- [12] E. Vedejs, N.S. Bennett, L.M. Conn, S.T. Diver, M. Gingras, S. Lin, P.A. Oliver, M.J. Peterson, *J. Org. Chem.* 56 (1993) 7286.
- [13] A.C. Cope, E.C. Herrich, *Organic synthesis collective, IV*, Wiley, New York, 1963, p. 304.
- [14] J. Iqbal, R.R. Srivastava, *J. Org. Chem.* 57 (1992) 2001.
- [15] G.W. Breton, M.J. Kurtz, S.L. Kurtz, *Tetrahedron Lett.* 38 (1997) 3825.
- [16] H. Hagiwara, K. Morohashi, T. Suzuki, M. Ando, I. Yamamoto, M. Kato, *Synth. Commun.* 28 (1998) 2001.
- [17] R. Ballini, G. Bosica, S. Carloni, L. Ciaralli, R. Maggi, G. Sartori, *Tetrahedron Lett.* 39 (1998) 6049.
- [18] S.V. Pansar, M.G. Malusare, A.N. Rai, *Synth. Commun.* 30 (2000) 2587.
- [19] I. Mohammadpoor-Baltork, H. Aliyan, A.R. Khosropour, *Tetrahedron* 57 (2001) 5851.
- [20] (a) S. Chandrasekar, T.S. Tin, Y.R. Ma, Z.H. Zhang, T.S. Li, *Synth. Commun.* 28 (1998) 3173; (b) T. Ramachander, M. Takhi, *Tetrahedron Lett.* 39 (1998) 3263.
- [21] T.S. Tin, Y.R. Ma, Z.H. Zhang, T.S. Li, *Synth. Commun.* 28 (1998) 3173.
- [22] T. Srikanth Reddy, M. Narasimhulu, N. Suryakiran, K. Chinni Mahesh, K. Ashalatha, y. Venkateswarlu, *Tetrahedron Lett.* 255 (2006) 78.
- [23] R.H. Tale, R.N. Adude, *Tetrahedron Lett.* 47 (2006) 7263.
- [24] P.A. Procopiou, S.P.D. Baugh, S.S. Flack, G.G.A. Inglis, *J. Org. Chem.* 63 (1998) 2342.
- [25] R. Qiu, G. Zhang, X. Ren, X. Xu, R. Yang, S. Luo, S. Yin, *J. Organomet. Chem.* 695 (2010) 1182.
- [26] M.L. Kantam, K. Aziz, P.R. Likhari, *Catal. Commun.* 7 (2006) 484.
- [27] R. Ghosh, S. Maiti, A. Chakraborty, *Tetrahedron Lett.* 46 (2005) 147.
- [28] A.K. Chakraborti, L. Sharma, A.K. Gulhane, R. Shivani, *Tetrahedron* 59 (2003) 7661.
- [29] R. Shivani, A.K. Gulhane, Chakraborti, *J. Mol. Catal. A Chem.* 264 (2007) 208.
- [30] A.K. Chakraborti, R. Gulhane, *Tetrahedron Lett.* 44 (2003) 3521.
- [31] A.K. Chakraborti, A.K. Gulhane, R. Shivani, *Synthesis* (2004) 111.
- [32] A.K. Chakraborti, A.K. Gulhane, *J. Chem. Soc. Chem. Commun.* (2003) 1896.
- [33] S. Tangestaninejad, M.H. Habibi, V. Mirkhani, M. Moghadam, *Synth. Commun.* 32 (2002) 1337.
- [34] M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, R. Shaibani, *J. Mol. Catal. A Chem.* 219 (2004) 73.
- [35] M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, S.A. Taghavi, *J. Mol. Catal. A Chem.* 274 (2007) 217.
- [36] J.K. Joseph, S.L. Jain, B. Sain, *J. Mol. Catal. A Chem.* 267 (2007) 108.
- [37] M. Curini, F. Epifano, M.C. Marcotullio, O. Rosati, M. Rossi, *Synth. Commun.* 30 (2000) 1319.
- [38] M. Barbero, S. Cadamuro, S. Dughera, P. Enturello, *Synthesis* (2008) 3625.
- [39] F. Shirini, M.A. Zolfigol, M. Abedini, *Monatsh Chem.* 140 (2009) 1495.
- [40] V. Mirkhani, S. Tangestaninejad, M. Moghadam, B. Yadollahi, L. Alipannah, *Monatsh Chem.* 135 (2004) 1257.
- [41] A.K. Chakraborti, A.K. Gulhane, R. Shivani, *Synlett* (2003) 1805.
- [42] (a) F. Rajabi, *Tetrahedron Lett.* 50 (2009) 395; (b) B.M. Choudary, M.L. Kantam, B. Bharathi, C. Reddy, V. Reddy, *J. Mol. Catal. A Chem.* 168 (2001) 69.
- [43] R. Alleti, M. Perambudura, S. Samantha, V.P. Reddy, *J. Mol. Catal. A Chem.* 226 (2005) 57.
- [44] A.K. Chakraborti, R. Gulhane, *Tetrahedron Lett.* 44 (2003) 6749.
- [45] A.T. Khan, L.H. Choudhury, S. Ghosh, *Eur. J. Org. Chem.* (2005) 2782.
- [46] M. Salavati-Niasari, S. Hydarzadeh, A. Amiri, S. Salavati, *J. Mol. Catal. A Chem.* 232 (2003) 191.
- [47] B. Karimi, J. Maleki, *J. Org. Chem.* 68 (2003) 4951.
- [48] (a) A. Rahmatpour, *Heteroat. Chem.* 22 (2011) 85; (b) A. Rahmatpour, *Heteroat. Chem.* 22 (2011) 51.
- [49] A. Rahmatpour, *J. Organomet. Chem.* 712 (2012) 15.
- [50] (a) A.P. Deshmukh, K.J. Padiya, M.M. Salunkhe, *J. Chem. Res. (S)* 9 (1999) 568; (b) I.M. Kolthoff, E.B. Sandell, *Textbook of Quantitative Inorganic Analysis*, Macmillan, New York (1965).
- [51] (a) D.C. Neckers, D.A. Kooistra, G.W. Green, *J. Am. Chem. Soc.* 94 (1972) 9284; (b) E.C. Blossey, L.M. Turner, D.C. Neckers, *J. Org. Chem.* 40 (1975) 959.