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Polymer-supported gadolinium triflate as a convenient and efficient Lewis acid catalyst for acetylation of alcohols and phenols

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Abstract

A polymer-supported gadolinium triflate (CMPS-IM-Gd) catalyst was prepared from chloromethyl polystyrene (CMPS) resin using a simple and convenient procedure. This polymeric catalyst was used as an efficient Lewis acid catalyst for the acetylation of various alcohols and phenols with acetic anhydride, affording high yields under mild conditions. The reaction was completed in a short period of time with small amounts of the catalyst. The catalyst was reused over 10 times without any significant loss of its catalytic activity.

Keywords: Polymer-supported catalyst; Acetylation; Gadolinium triflate; Lewis acid catalyst

Functional group manipulations through protection and deprotection strategies are highly essential in organic synthesis and extensively used in the preparation of multifunctional organic compounds. Among various protecting methods, acetylation is one of the most frequently used functional group transformations.[1–3] The acetylation of alcohols and phenols is typically performed using acetic anhydride with the aid of either base or acid catalysts. Some of the base catalysts are toxic, flammable and possess offensive odours.[4] Protic acids are also known to catalyze the acetylation process.[5] However, some of these catalysts are not entirely satisfactory due to the instability of reactants or products under the reaction conditions and the time-consuming work-up procedures. In addition, several Lewis acids, including simple metal salts,[6] metal triflates[7] and others,[8] have been used as catalysts for these transformations. Although various acetylation methods are available, most of the aforementioned methods have one or more drawbacks, which include long reaction times, harsh reaction conditions and often, poor yields of the desired products. Furthermore, most of the metal triflates are rather expensive and some of them must be used under critically anhydrous conditions for optimum results. Also, most of the catalysts are usually used in environmentally harmful organic solvents, thereby generating large amounts of corrosive and toxic waste products. One of the most promising solutions to this problem appears to be the immobilization of the soluble catalysts onto an insoluble matrix, without any reduction of catalytic performance (activity and selectivity, etc.) with respect to the homogeneous ones. Consequently, in recent years, some of the supported acid catalysts have received much attention for their reusability, increasing reactivity, ease of handling as well as for their environmental and economic advantages.[9] However, some of them still require high reaction temperatures, tedious work and high preparation costs.

Very recently, $Gd(OTf)_3$ was used as a water-tolerant Lewis acid in the aldol reaction[10] as well as the acetylation of alcohols and amines.[11] It is not only more water-tolerant

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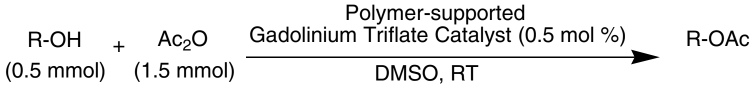
than other lanthanide based metal triflates but also milder and inexpensive. Previously, we have demonstrated the advantages of various polymer-supported catalysts in organic synthesis.[12] In continuation of our ongoing studies on polymer-supported catalysts, we found that immobilized $Gd(OTf)_3$ could be an effective Lewis acid catalyst. Herein, we now report a polymer-supported gadolinium triflate catalyst as a new, milder and efficient recyclable heterogeneous catalyst for the acetylation of alcohols and phenols (Scheme 1).

Our design for the preparation of polymer-supported gadolinium triflate catalyst is depicted in Figure 1. The imidazolium-loaded ionic liquid resin for the immobilization of gadolinium triflate was synthesized from Merrifield resin (CMPS, 1.80 mmol Cl/g) by treating with 1.5 equiv of 1-methylimidazole in DMF at 80 °C for 12 h. The loading of imidazolium group was 1.42 mmol/g, which was determined by nitrogen analysis. The imidazolium-loaded ionic liquid was then treated with potassium *t*-butoxide, which acted as a base for the in situ deprotonation of imidazolium salts. After washing out extra unreacted base, $Gd(OTf)_3$ was then treated with CMPS-IM to give the desired polymer-supported gadolinium triflate (CMPS-IM-Gd) catalyst. The loading level of Gd was 0.05 mmol/g, which was determined by inductively coupled plasma-atomic emission spectrometry (ICP-AES). This means that 3.52% of the imidazoium functionality on the resin participated in the Gd complex formation. In addition, the gadolinium complex formation was confirmed by energy dispersive X-ray spectroscopy (EDX) and FT-IR spectroscopy. The surface morphology of the catalyst was characterized by field emission scanning electron microscope (FE-SEM).[13]

As shown in Figure 2, the swelling volume of the CMPS-IM-Gd catalyst was measured. The catalytic activity was then evaluated using the acetylation of alcohols and phenols as a model reaction. Since the solvent employed may influence the catalytic activity of the CMPS-IM-Gd catalyst, a variety of solvents were tested using benzylalcohol as a model substrate (Table 1). As expected, the catalytic activity of the CMPS-IM-Gd catalyst was well correlated



Scheme 1.

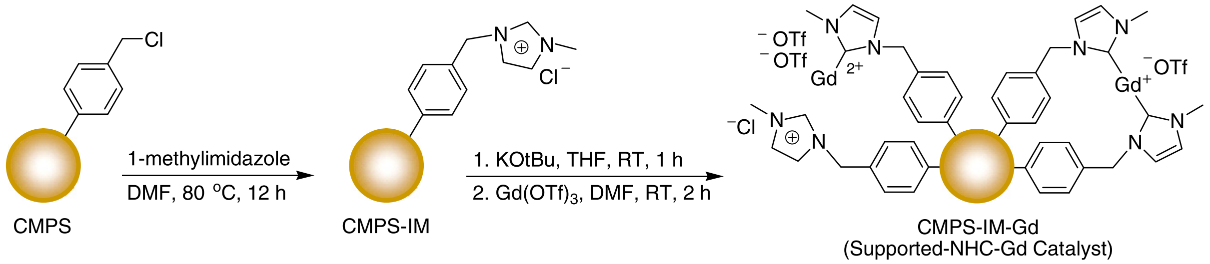


Fig. 1. Preparation of the CMPS-IM-Gd catalyst.

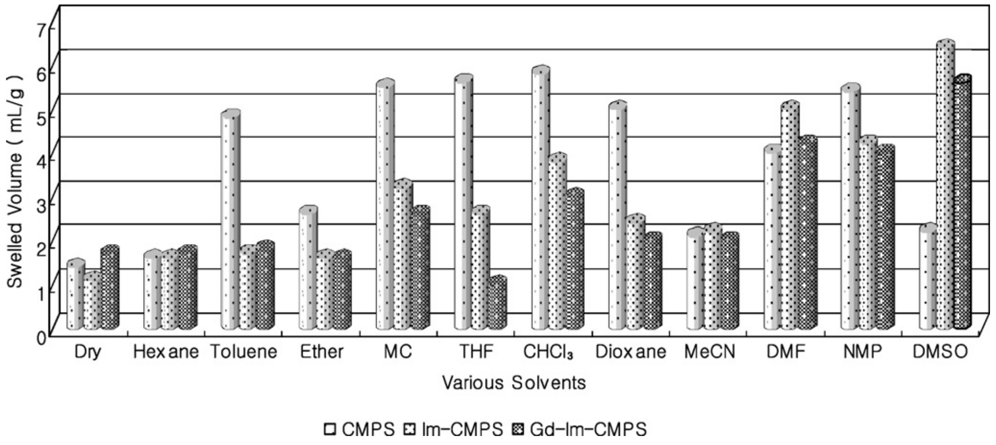
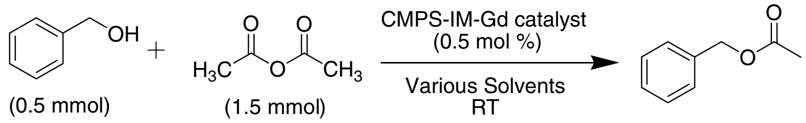


Fig. 2. Swelling volume of the CMPS-IM-Gd catalyst. The swelling volumes of the polymer-supported gadolinium triflate in various solvents were measured in a fritted column (ID 1 cm, length 15 cm). The resins (1.0 g) were swollen in a solvent at rt for 30 min, and then washed. The resin volume was measured after filtering out the solvent.

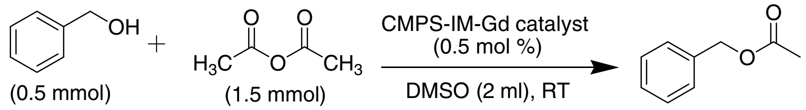
Table 1
Effects of solvent on the acetylation of benzyl alcohol



Rxn. time (h)	Conversion[a] (%)										
	Hexane	Toluene	Ether	MC	THF	$CHCl_3$	Dioxane	MeCN	DMF	NMP	DMSO
2	78	38	78	24	41	23	32	50	90	88	>99
3	91	58	77	42	66	43	52	75	>99	>99	>99

[a] Conversions were determined by GC/MS.

Table 2
Conversion of benzyl alcohol in the presence of the catalyst and in the absence of the catalyst



Entry	Amount of catalyst (mol %)	Conversion[a] (%) at a given reaction time								
		1 min	5 min	10 min	20 min	30 min	45 min	60 min	90 min	120 min
1	None	—	—	—	2	4	4	6	7	13
2	0.1	—	5	6	9	11	13	17	24	28
3	0.5	17	27	40	68	69	82	88	>99	>99
4	1.0	24	41	84	89	>99	>99	>99	>99	>99

[a] Conversions were determined by GC/MS.

to the swelling property of the solvent employed. The catalyst displayed the largest swelling volume and the highest activity in polar aprotic solvents such as DMF, NMP and DMSO. As shown in Table 2, the amounts of catalyst were also varied in order to monitor the progress of reaction versus time. In the absence of catalyst, no appreciable amount of the corresponding products was detected even after prolonging the reaction time up to 24 h (entry 1). By increasing the amount of the CMPS-IM-Gd catalyst, the acetylation was shown to be greatly accelerated (entries 2–4). When 1.0 mol % of the catalyst was employed, the reaction was completed in less than 30 min (entry 4) at room temperature.

On the basis of these results, we next investigated the scope of the substrate alcohols including phenols with regard to the CMPS-IM-Gd catalyst-mediated acetylation, and the results obtained are summarized in Table 3. To examine the utility of this catalyst, a wide range of alcohols including *primary* (acyclic, and benzylic), *secondary* (acyclic, cyclic and benzylic) and sterically hindered *tertiary* alcohols were evaluated as substrates. The reactivity of the substrate alcohol was greatly dependant on the steric factor. Most of the *primary* and *secondary* alcohols were easily converted to their corresponding acetate, with good to excellent yields (entries 1–10). However, in the cases of employing *tertiary* or sterically demanding alcohols, low conversion was observed even after prolonging the reaction time (entries 12–15, 18). When the reaction conditions such as the amount of catalyst or the reaction temperature were changed, the above-mentioned compounds were acetylated in higher yields (entries 16–18). As shown in Table 4, a series of phenols were also examined, and their conversions to their acetyl products gave similar results under the same conditions.

The stability of the catalyst and its reusability are the main advantages of this polymeric catalyst. The CMPS-IM-Gd catalyst could be stored and handled under open-air conditions. Furthermore, the catalyst was quantitatively recovered by simple washing and filtration methods, and proved to be reusable up to 10 times without any loss of appreciable amount of catalytic activity (Table 5). In most cases of employing different types of selected substrates, the conversions at a given reaction time were almost same as those obtained in the first use. The extent of Gd ion leaching from the catalyst was very low as judged by ICP-AES analysis. After the 2nd run to the 10th run, the Gd contents in the recovered catalyst were remained almost the same.

In conclusion, we have described an easy and novel method for the immobilization of gadolinium triflate on a polymer matrix. The resulting CMPS-IM-Gd catalyst was found to be air-stable, non-volatile and much easier to handle than its soluble counterpart, $Gd(OTf)_3$. This complex was evaluated as a heterogeneous catalyst for the acetylation of alcohols and phenols with acetic anhydride, and exhibited super activity over a wide range of substrates.

Table 3
Acetylation of various alcohols

$$\underset{(0.5\ \text{mmol})}{\text{R-OH}} + \underset{(1.5\ \text{mmol})}{\text{Ac}_2\text{O}} \xrightarrow[\text{DMSO (2 ml), RT}]{\substack{\text{CMPS-IM-Gd catalyst}\\(0.5\ \text{mol \%})}} \text{R-OAc}$$

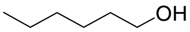
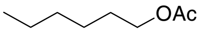
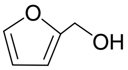
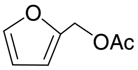
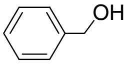
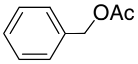
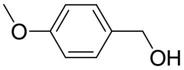
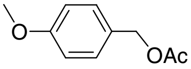
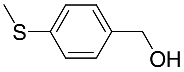
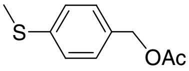
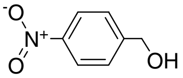
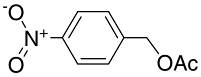
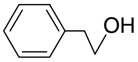
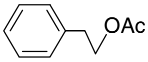
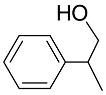
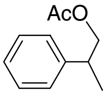
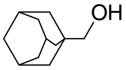
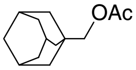
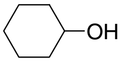
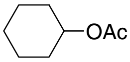
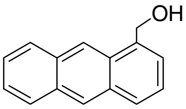
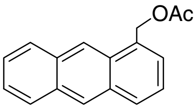
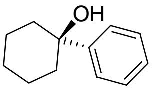
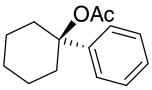
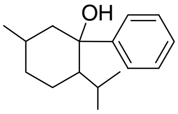
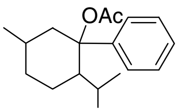
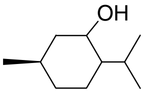
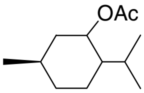
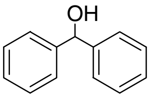
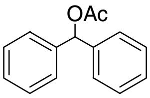
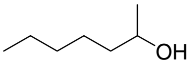
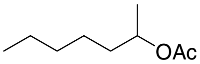
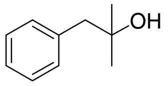
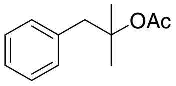
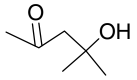
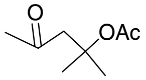
Entry	Alcohol	Acetate	Time	Yield[a] (%)
1			5 min	94
2			5 min	94
3			1.5 h	>99
4			1 h	97
5			1.5 h	>99
6			1 h	97
7			5 h	96
8			12 h	63
9			6 h	52
10			5 min	>99
11			6 h	93
12			24 h	14
13			24 h	17
14			24 h	18
15			24 h	31
16			24 h	62[b]

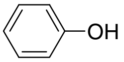
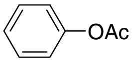
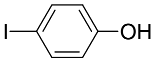
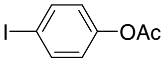
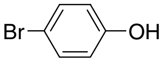
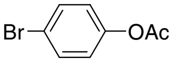
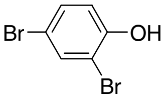
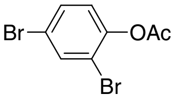
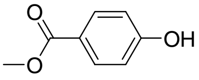
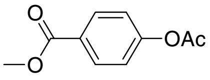
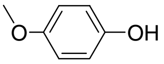
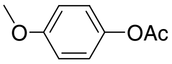
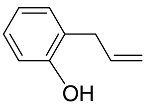
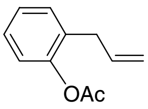
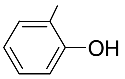
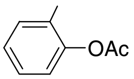
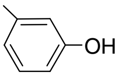
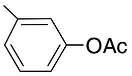
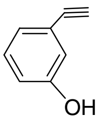
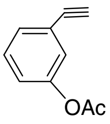
Table 3 (*continued*)

Entry	Alcohol	Acetate	Time	Yield[a] (%)
17			24 h	27[d]
18			24 h	22 (38)[c]

[a] Yields were determined by GC/MS.
[b] 1 mol % of catalyst was used at room temperature.
[c] 3 mol % of catalyst was used at room temperature.
[d] 3 mol % of catalyst was used at 50 °C.

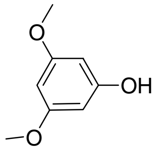
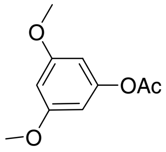
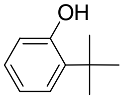
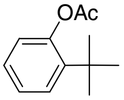
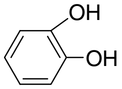
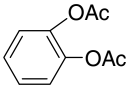
Table 4
Acetylation of various phenols

$$\underset{(0.5\ \text{mmol})}{\text{R-OH}} + \underset{(1.5\ \text{mmol})}{\text{Ac}_2\text{O}} \xrightarrow[\text{DMSO (2 ml), RT}]{\text{CMPS-IM-Gd catalyst (0.5 mol \%)}} \text{R-OAc}$$

Entry	Phenol	Acetate	Time	Yield[a] (%)
1			5 min	94
2			3 min	92
3			3 min	91
4			3 min	>99
5			5 min	93
6			10 min	95
7			45 min	97
8			30 min	>99
9			15 min	91
10			5 min	99

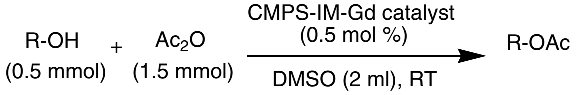
(*continued on next page*)

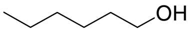
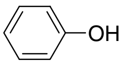
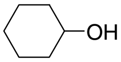
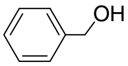
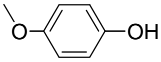
Table 4 (*continued*)

Entry	Phenol	Acetate	Time	Yield[a] (%)
11			5 min	93
12			1 h	96
13			5 min	95

[a] Yields were determined by GC/MS.

Table 5
Recycling of the CMPS-IM-Gd catalyst



Entry	Alcohols and phenols	Rxn. time	Conversion[a,b] (%)									
			1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
1		5 min	94	97	>99	>99	>99	>99	>99	>99	>99	>99
2		5 min	94	92	>99	96	94	>99	>99	>99	>99	>99
3		10 min	>99	97	93	94	97	>99	91	>99	>99	>99
4		2 h	>99	98	93	94	>99	>99	90	>99	>99	98
5		5 h	95	93	96	96	97	93	92	>99	>99	>99

[a] Conversions were determined by GC/MS.

[b] After the reaction, the mixture was filtered and washed with aq Na$_2$CO$_3$ solution, diethyl ether and brine. The catalyst was reused after drying.

Furthermore, the catalyst could be easily recovered by simple washing and filtration and could be reused up to 10 times without significant loss in its catalytic activity. These results suggest the increased potential of the CMPS-IM-Gd catalyst to be used as a novel Lewis acid catalyst in various organic reactions as well as industrial applications. Studies involving the use of immobilized gadolinium triflate catalyst in other Lewis acid-mediated reactions are currently underway in our laboratory and will be reported in due course.

Acknowledgements

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Tributylphosphine: (c) Vedejs, E.; Diver, S. T. *J. Am. Chem. Soc.* **1993**, *115*, 3358; PPY (4-pyrrolidinopyridine): (d) Scriven, E. F. V. *Chem. Soc. Rev.* **1983**, *12*, 129; TEA (Triethylamine): (e) Zhdanov, R. I.; Zhenodarova, S. M. *Synthesis* **1975**, 222.

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13. The gadolinium complex formation was confirmed by energy dispersive X-ray spectroscopy (EDX). We confirmed that palladium was immobilized specifically at the C2 position of the imidazolium on the bead with FT-IR spectroscopy. Before immobilization of palladium, a strong band of quaternary imidazolium on the bead appeared at 1157 cm^{-1} in the IR spectrum.[11] However, it decreased, and the band of alkene at 1665 cm^{-1} became stronger after immobilization of palladium. Also, the surface morphology of the catalyst was characterized by field emission scanning electron microscope (FE-SEM). There is no difference between before immobilization of gadolinium triflate and after.