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COMMUNICATION

Ionic Liquid Brush as an Efficient and Reusable Heterogeneous Catalytic Assembly for Tosylation of Phenols and Alcohols in Neat Water

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A very efficient and reusable heterogeneous assembly of ionic liquid brush has been developed. The catalyst exhibits high catalytic activity for tosylation of phenols and alcohols in neat water. Moreover, the catalyst shows outstanding stability and reusability, and it can be recovered simply and effectively and reused five times without noticeable loss of the catalytic activity.

The *p*-toluenesulfonylation (tosylation) of alcohols and phenols has long been recognized as fundamental processes in various fields of organic syntheses.[1-3] The resulting tosylates are useful building blocks as well as key intermediates in organic synthesis[4-9] and various tosylates have important pharmacological properties.[10-13] In the past decate, impressive efforts have been devoted to prepare tosylates utilizing various reaction systems involved solvent-free synthesis,[14-16] heteropolyacid[17] or metal-catalyzed[18-21] tosylation, and reaction of alcohols with *p*-toluenesufonic acid (*p*-TsOH) using silica chloride[22] or $CoCl_2{\cdot}6H_2O$[23] as catalyst. The most common procedure for the construction of tosylates is treatment of alcohols and phenols with *p*-toluenesulfonyl chloride (*p*-TsCl) in the presence of an amine base, such as pyridine,[3] $Et_3N/Me_3N{\cdot}HCl$, [24] $Me_2N(CH_2)_nNMe_2$[25]or DABCO[26-27] in an anhydrous organic solvent such as dichloromethane, acetonitrile or toluene. Although the reaction systems were well designed, these methods suffer from difficulty in excess amount of amine, undesired side reaction, complex workup procedures and organic solvents, which would lead to chemical waste.

Over the past few years, considerable attention has been paid to water-solvent reactions from the standpoint of green chemistry.[28-32] However, water is still not commonly used as the sole solvent for organic transformations in the laboratory and in industry due to the limited water solubility of organic substrates.[33] In the past decade, although there have been several synthetic methods for tosylation of phenols and alcohols, to the best our knowledge, the reported procedures for these variants in water to date have been rather routine. Tanabe[34] reported an effective tosylation of alcohols in water promoted by KOH and catalytic amines, but it required control of the pH of water to prevent hydrolysis of *p*-TsCl (Figure 1a). Another procedure reported by Matsubara[35] with *N*-hexadecylimidazole as an efficient homogenous catalyst in water seems to be attractive, because they supposed that aggregation of the amphiphilic catalyst carrying a hydrophobic methylene chain would work as a substitute for organic solvent (Figure 1b). However, the catalyst was difficult to separate from the reaction product, which limits its recycling. Thus there is still a need to develop more efficient and environmentally friendly catalysts and procedures for the tosylation transformations.

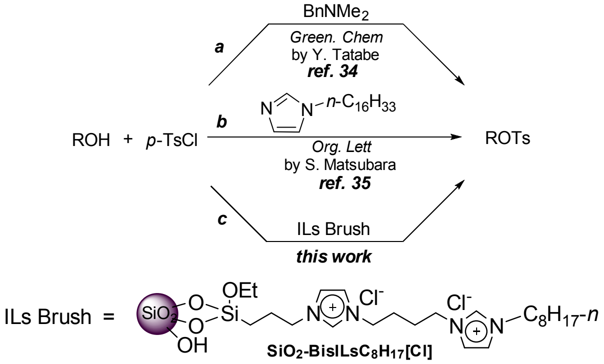

Fig. 1. Tosylation of phenols and alcohols in neat water.

Recently, our group designed and synthesized a series of SiO_2-supported bis-layered ionic liquids (ILs) bearing two imidazolium ions on each of the side chains. We call them

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"ionic liquid brushes" because of their brush-like feature (Figure 1c). The brush extends the immobilized ILs to the upper spaces outside the surface of SiO_2, forming an immobilized bis-layered ILs possessing more prominent 3D characters resembling that of the free ionic liquids. In comparison with the monolayer ILs, we expect our immobilized bis-layered ILs, should act as highly active catalysts, cocatalysts or supports based on the following points: (1) deeper 3D microenvironment and more flexibility of the longer branched chains containing imidazoliums for more molecules of substrates and reagents to be accommodated; (2) adjustable hydrophobicity for the substrates and reagents to "be dissolved" in and for the product and side-product to move out of the brushes, and (3) ability to perform the reaction under organic solvent-free condition or in water without the addition of any phase transfer catalysts. Based upon such an idea, we have found that the ionic liquid brush displayed excellent activity and excellent reusability in several organic transformations with water as a sole solvent.[36-37]Herein, we wish to describe our preliminary results of the brush as an efficient and reusable catalyst for tosylation of phenols and alcohols in water.

The brush catalyst SiO_2-BisILsC_8H_{17}[Cl] was synthesized through a three-step route according to the procedure we previously reported.[36-37] The catalyst of ionic liquid brushes assembly was prepared via coordination linkage between immobilized ionic liquid brushes using cheap SiO_2 as supporter. BET analysis showed the brush has a S_{BET} of 181 m^2/g. Elemental analysis reveals that there are 1.27 mmol/g of imidazolium ions loaded on the dilayer ionic liquid brush, nearly two times the amount of imidazolium ions on its monolayer analogue. The brush is stable to air and moisture.

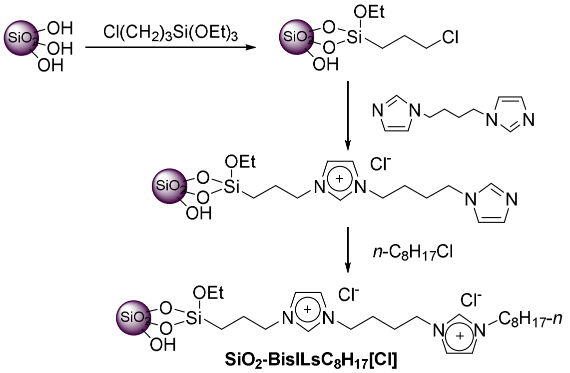
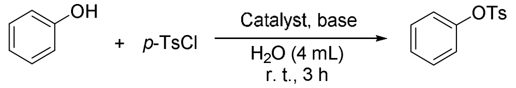


Fig 2. Synthetic route of the brush catalyst.

Initially, we employed the tosylation reaction of phenol with *p*-TsCl as a prototypical reaction for discovery of suitable reaction conditions and the examination of the catalytic activity in neat water. All of the reactions were carried out by simply stirring a mixture of the catalyst, phenol, *p*-TsCl and a base in neat water at room temperature for 3 h; no any organic co-solvents or other additives were employed. The results are listed in Table 1.

Table 1. The brush-catalyzed tosylation of phenol with *p*-TsCl in water under various conditions.[a]



Entry	Catalyst (mol%)[b]	Base	Yield (%)[c]
1	-	Na_2CO_3	52
2	0.5	Na_2CO_3	74
3	1.0	Na_2CO_3	85
4	1.5	Na_2CO_3	95
5	**2.0**	**Na_2CO_3**	**99**
6	2.0	$NaHCO_3$	68
7	2.0	NaOH	84
8	2.0	Et_3N	63
9	2.0	DABCO	72
10[d]	10	K_2CO_3	80

[a] Conditions: phenol (2 mmol), *p*-TsCl (2.4 mmol), base (2 mmol), H_2O (4 mL) with the brush as catalyst. [b] Based on the imidazolium ions. [c] Isolated yield. [d] *N*-exadecylimidazole as catalyst reported in literature.[35] DABCO = 1,4-Diazabicyclo[2.2.2]octane.

As can be seen, the present brush catalyst with *n*-octyl as the terminal alkyl group was efficient for the tosylation of phenol with *p*-TsCl in water. In sharp contrast, the control experiment without the catalyst gave the corresponding product in a rather low yield of 52%, which indicated that the catalyst played an important role in the reaction (Table 1, Entry 1). The yields of product increased with the addition of catalyst (Table 1, Entry 2-5). A loading of 2.0 mol% (2 mmol imidazolium loaded on the brush catalyst/100 mmol substrate) of the brush catalyst showed great efficiency to the reaction, giving the desired product in nearly quantitative yield without detectable unwanted product (Table 1, Entry 5), in contrast to the reported yield of 80% for the same reaction catalyzed by 0.1 equiv. (10 mol% with respect to substrate) of *N*-hexadecylimidazole in water (Table 1, Entry 10)[35]. Other bases such as $NaHCO_3$, NaOH, Et_3N and DABCO were also investigated, but lower yields of the products were obtained (Table 1, Entry 6-9). Finally, the most suitable reaction conditions were defined as 1.2 equivalents of *p*-TsCl to phenols or alcohols in the presence of 1 equivalents of Na_2CO_3 as an inorganic base under 2.0 mol% of the catalyst at room temperature for 3 h.

To investigate the catalytic ability of the brush to act as catalysts on the tosylation of phenols and alcohols, different phenols and

Table 2 Organic solvent-free tosylation of phenols with the brush as a catalyst.[a]

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Entry	R	Yield (%)[b]
1	H	99
2	4-CH_3	94
3	4-Cl	99
4	2-NO_2	91
5	4-NO_2	92
6[c]	4-OH	96
7		94

[a] conditions: The brush (0.04 mmol, based on imidazolium ions), phenol (2 mmol), *p*-TsCl (2.4 mmol), Na_2CO_3 (2 mmol), H_2O (4 mL). [b] Isolated yields. [c] The brush (0.08 mmol, based on imidazolium ions), alcohol (2 mmol), *p*-TsCl (4.8 mmol), Na_2CO_3 (4 mmol), H_2O (4 mL).

alcohols were mixed with *p*-TsCl in the presence of the brush to form the tosylates in neat water. As shown in Table 2, various phenols bearing electron-donating or electron-withdrawing substituents were applied to this protocol and the desired products were obtained in good to excellent yields.

Under this organic solvent-free condition, a series of alcohols were next pursued with *p*-TsCl into the corresponding tosylates. As shown in Tables 3, by using the brush as the catalyst, primary, secondary, benzylic alcohols were all successfully converted to the corresponding tosylates. In the case of the aliphatic alcohols, primary alcohols were tosylated in excellent yields compared to secondary alcohols. For example, 1-pentanol, 3-methyl-1-butanol, 1-hexanol, 1-octanol, cyclohexylmethanol and 2-phenylethanol were transformed into the corresponding tosylates in 66-91% yields (Table 3, entries 4-6, 8, 10 and 14), whereas cyclohexanol and 2-octanol were less reactive, which afforded tosylates in only 55% and 82% yields, respectively (Table 3, entry 7 and 9). We attribute the low yields of ethanol, 1-butanol and 2-butanol to their solubility in water (Table 3, entries 1-3). Due to the mild reaction conditions, dihydric alcohols also afforded the corresponding tosylates (Table 3, entries 11-13). For unsymmetric diol, such as butane-1,3-diol, when 2.4 equivalents of *p*-TsCl was used, afforded the corresponding product at both primary and secondary side in 49 % yield; when 1.2 equivalents of *p*-TsCl was used, the tosylate almost generated at the primary side in 61 % yield. Benzylic alcohols, such as benzyl, 4-hydroxybenzyl, 4-chlorobenzyl, 2-bromobenzyl, 4-bromobenzyl, 2-nitrobenzyl, 4-nitrobenzyl alcohols were all converted to the corresponding tosylates in 61%-95% yields (Table 3, entries 15-21). However, tertiary alcohol such as *t*-BuOH was converted to the corresponding tosylate in less than 10% yield, along with some undesired impurities, which lead to difficult to isolate and purify the final product.

Table 3 Organic solvent free tosylation of alcohols with the brush as a Catalyst.[a]

Entry	ROH	Yield (%)[b]
1		42
2		57
3		54
4		69
5		66
6		79
7		55
8		91
9		82
10		73
11		49[c]
12		66[c]
13		49[c] 61[a]
14		81
15	R = H	61
16	R = 4-OH	95[c]
17	R = 4-Cl	77
18	R = 2-Br	80
19	R = 4-Br	82
20	R = 2-NO_2	89
21	R = 4-NO_2	92

[a] Conditions: The brush (0.04 mmol, based on imidazolium ions), alcohol (2 mmol), *p*-TsCl (2.4 mmol), Na_2CO_3 (2 mmol), H_2O (4 mL). [b] Isolated yields. [c] The brush (0.08 mmol, based on imidazolium ions), alcohol (2 mmol), *p*-TsCl (4.8 mmol), Na_2CO_3 (4 mmol), H_2O (4 mL).

The present heterogeneous catalysts have an advantage that at the end of reaction the catalyst can be removed from the reaction stream by simple filtration. To investigate the recyclability of the brush, we carried out the reaction of phenol with *p*-TsCl repeatedly under the optimized conditions. It is noteworthy that at the end of the reaction the present catalyst can be recovered by a simple filtration of the reaction solution and recycled five times. In every case, the catalyst was only recovered by filtration and washed with ethyl acetate and water, then the experiment repeated. The result showed almost no significant reduction in high yields (96-99 %) (Figure 3). Elemental analysis reveals that the brush catalyst after 5th cycle has nearly the same content of nitrogen on the brush. The infrared spectral analysis shows the main absorption peaks remain unchanged as compared with the fresh catalyst. All these results indicate the brush catalyst is stable

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in the reaction. The high recyclability of this catalytic system allows for a more economic and environmentally friendly process.

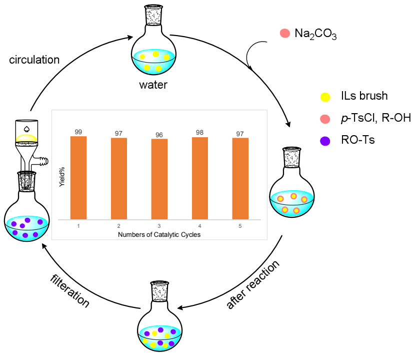

Figure 3. The recycling of catalyst in the tosylation of phenol.

In conclusion, ionic liquid brush has been shown to be an efficient heterogeneous catalyst for tosylation of phenols and alcohols with *p*-TsCl in neat water. The high efficiency, simplicity of the product isolation, outstanding recyclability, and organic solvent-free and water alone condition makes the catalyst and the process available in academic laboratories and could find industrial applications in the future.

Acknowledgements

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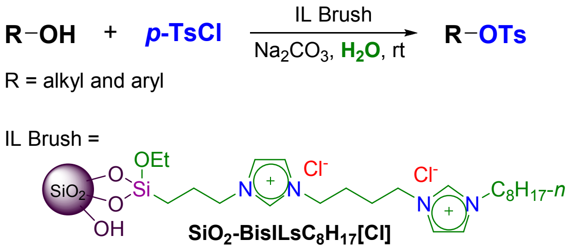
Ionic Liquid Brush as an Efficient and Reusable Heterogeneous Catalytic Assembly for Tosylation of Phenols and Alcohols in Neat Water



An efficient and reusable heterogeneous catalytic assembly-ionic liquid brush was developed for tosylation of phenols and alcohols in neat water.