RESEARCH LETTER

Long-chain double SO$_3$H-functionalized Bronsted acidic ionic liquids catalyzed selective alkylation of phenol and p-cresol with tert-butanol

Xinzhong Li$^{a,b,*}$, Rong Cao$^{a}$ and Qi Lin$^{b}$

$^{a}$State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou, P.R. China; $^{b}$Department of Chemistry and Chemical Engineering, Minjiang University, Fuzhou, P.R. China

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A simple, efficient, and selective approach for the tert-butylation of phenol and p-cresol using two double SO$_3$H-functionalized long-chain Bronsted acidic ionic liquids as recyclable catalysts is reported. Under optimum reaction conditions, 89.4% conversion of the phenol and 73.7% selectivity of 2,4-tert-butyl-phenol and 93.2% conversion of the p-cresol and 89.2% selectivity of 2-tert-butyl-p-cresol were obtained. Two ionic liquids could be recovered readily and their catalytic activity almost completely retained after five recycles.

**Keywords**: ionic liquid; Bronsted acid; phenol; p-cresol; tert-butylation

Introduction

Alkylation of phenol and cresol with tert-butyl alcohol (TBA) is a typical acid-catalyzed Friedel–Crafts reaction, and it is widely used in the manufacture of pharmaceuticals and fine chemicals (1–3). Homogenous and heterogeneous catalysts were developed for this transformation. For example, AlCl$_3$, FeCl$_3$, and ZnCl$_2$ (4), H$_2$SO$_4$, H$_3$PO$_4$, HF, HClO$_4$ (5), mesoporous materials (6–8), heteropoly acids (9), zeolites (10), cation exchange resin (11), sulfated zirconia (12), polymer-supported sulfonamide (13), silica supported Al (14), and transition metal oxides (15), and so on. Based on the standards of green chemistry, these procedures are suffering from disadvantages, such as corrosion equipments, lack of selectivity, environmental pollution, complex processes and difficult work-ups, catalyst with high cost or poor thermal stability, prone to deactivation, etc. Thus, developing environmentally benign, highly selective, and efficient alternatives is highly desirable. Recently, single SO$_3$H-functionalized Bronsted acidic ionic liquids (BAILs) acting as environment friendly and recyclable catalysts have been successfully applied in selective alkylation p-cresol and phenol with TBA (16–18). These reported methods demonstrated some advantages such as high conversion and selectivity, mild reaction conditions, ionic liquids could be reused after simple treatment, and so on. But these reported ionic liquids were limited by their lower acidity and high cost for potential industrial application. Herein we wish to report a simple, efficient, and selective approach for tert-butylation phenol and p-cresol with TBA using two novel double SO$_3$H-functionalized long-chain BAILs-1 and -2 (Figure 1) as reusable catalysts. Under optimum reaction conditions, p-cresol and phenol reacted with TBA smoothly under mild reaction conditions and gave high conversion and selectivity of 2-tert-butyl-p-cresol (2-TBC) and 2,4-di-tert-butyl-phenol (2,4-DTBP) (Figure 2). On completion, two ionic liquids could be easily recycled and reused for five times successively without notable decrease in their catalytic activity.

Results and discussion

BAILs-1 and -2 were synthesized using commercially available N,N,N′,N″-tetramethylethylenelamine diamine, N,N,N′,N″,N‴-pentamethyldiethylenetriamine, and 1,3-butanenelulose as starting materials via quaternization and acidification in the two-step atom economic reactions. BAILs-1 and -2 exhibited higher acidity than H$_2$SO$_4$ and single SO$_3$H-functionalized BAIL-3 (16), BAIL-4 (17), and BAIL-5 (17) due to the double sulfonic acid groups on cations and two or three acidic HSO$_4^{-}$ anions in their structure (Table 1). The content of water in BAILs-1 and -2 ranges from 2.0% to 2.5% (Karl–Fischer titration). BAILs-1 and -2 both showed good thermal stability. Their thermal decomposition temperature is 523 K and 533 K, respectively.

*Corresponding author. Email: bails_wl@126.com

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Figure 1. Synthetic route of long-chain double SO$_3$H-functionalized BAILs-1 and 2.

BAILs = 3HSO$_4$ (BAILs-3)  N  N  HSO$_4$ (BAILs-4)  N  N  N  SO$_3$H (BAILs-5)

H$_2$SO$_4$

Conversion: 85.8-89.4%

Selectivity to 2,6-DTBC 10.3-11.5%

Selectivity to 2-TBC 86.1-89.2%

Figure 2. Alkylation of phenol and p-cresol with TBA catalyzed by long-chain double SO$_3$H-functionalized BAILs-1 and 2.
Initially, the alkylation of p-cresol with TBA was chosen as model reaction, under optimum reaction conditions; BAILs-1 and -2 both showed high catalytic activity and selectivity for tert-butylation (Table 2, entries 1–2). These good results could be attributed to the high Brønsted acidity of BAILs-1 and -2, which not only promoted the formation of tert-butyl cation but also accelerated the O-alkylated product transferred into C-alkylated product rapidly. On the other hand, which also cause the alkylation reaction carried out at lower reaction temperature and completed within shorter time. For the purpose of comparison, single SO$_3$H-functionalized BAILs-3 and -5, solid acid TPA/TiO$_2$ (19), WO$_3$/ZrO$_2$ (19), and H$_2$SO$_4$ used as catalysts under the same reaction conditions were investigated (Table 2, entries 3–8). Considering both the conversion of p-cresol and the product distribution, BAILs-1 and 2 gave the best results. This indicated that the high acidity of catalyst is favorable for the enhancement of the conversion of p-cresol and the selectivity of 2-TBC. Moreover, for an acid catalyst with acidity higher than H$_2$SO$_4$ does not lead to further alkylation of 2-TBC with TBA. The influence of reaction temperature and time on the conversion and selectivity are shown in Tables 3 and 4. With the increasing of temperature, the conversion of p-cresol and the selectivity of 2-TBC first increase and then reach a maximum at 343 K. While the selectivity of 2,6-DTBC increases gradually. This indicated that the increase in temperature mainly cause the O-alkylated product turned into 2-TBC and further C-alkylation of 2-TBC with TBA. With the increasing of reaction time, the selectivity of 2,6-DTBC increase rapidly and reach a maximum after 6 h. Continued to increase in reaction time, the selectivity of 2,6-DTBC improves gradually, but the conversion of p-cresol almost remains constant, which agrees with the results reported in literature (16, 17). The influence of amount of BAILs on the conversion of p-cresol and

| Table 1. Hammett acidity function of BAILs-1 and -2. |
|-----------------------------------------------|
| **Entry** | **Con. (mol/l)** | **Amax** | **[%]** | **[B]** | **[BH]+** | **%** | **H$_0$** | **H$_0$** |
| 0.016     | 1.125 | 0.855 | 78.07 | 63.85 | 21.93 | 36.15 | 1.54 | 1.24 | 1.62 |
| 0.032     | 0.823 | 0.693 | 57.11 | 51.53 | 42.89 | 48.47 | 1.11 | 1.02 | 1.20 |
| 0.048     | 0.649 | 0.599 | 45.40 | 44.73 | 45.60 | 55.27 | 0.91 | 0.87 | 1.09 |
| 0.064     | 0.555 | 0.509 | 38.51 | 38.07 | 61.49 | 61.93 | 0.79 | 0.77 | 1.07 |

Note: $H_0 = PKa + \log[B]/[BH]+$, 4-nitroaniline $PKa = 0.99$; $H_0^1$ Hammett function of H$_2$SO$_4$.

| Table 2. Results of alkylation of p-cresol with TBA using various catalysts. |
|-----------------------------------------------|
| **Entry** | **Catalyst** | **Conversion of p-cresol (%)** | **Selectivity** |
| 1         | BAIL-1      | 87.7 | 86.1 | 11.5 | 1.4 |
| 2         | BAIL-2      | 93.2 | 89.2 | 10.3 | 1.5 |
| 3         | BAIL-3      | 82.6 | 80.5 | 16.7 | 2.8 |
| 4         | BAIL-4      | 80.7 | 90   | 9.5  | 0.5 |
| 5         | BAIL-5      | 80.0 | 91   | 8.9  | 0.1 |
| 6         | H$_2$SO$_4$ | 68.3 | 71.3 | 1.2  | 27.3 |
| 7         | TPA/TiO$_2$ | 82.0 | 87.0 | 9.0  | 4.0 |
| 8         | WO$_3$/ZrO$_2$ | 70  | 92.0 | 7.0  | 1.0 |

Note: Reaction conditions: p-cresol, 5 mmol; TBA, 5 mmol; catalyst, 5 mmol; cyclohexane, 3 mL; reaction temperature, 70°C; reaction time, 7 h.

| Table 3. Effect of the reaction temperature on the tert-butylation of p-cresol. |
|-----------------------------------------------|
| **Entry** | **Temperature (°C)** | **Conversion of p-cresol (%)** | **Selectivity** |
| 1         | 50        | 58.3 | 50.4 | 0  | 49.6 |
| 2         | 60        | 62.5 | 75.6 | 0  | 24.6 |
| 3         | 70        | 93.2 | 89.2 | 10.2 | 0.6 |
| 4         | 80        | 92.7 | 87.8 | 11.7 | 0.5 |
| 5         | 90        | 91.3 | 90.2 | 9.3  | 0.5 |

Note: Reaction conditions: p-cresol, 5 mmol; TBA, 5 mmol; BAIL-2, 5 mmol; cyclohexane, 3 mL; reaction time, 7 h.

| Table 4. Effect of the reaction time on the tert-butylation of p-cresol. |
|-----------------------------------------------|
| **Entry** | **Time (h)** | **Conversion of p-cresol (%)** | **Selectivity** |
| 1         | 3          | 57.4 | 79.3 | 0  | 20.7 |
| 2         | 4          | 62.5 | 75.6 | 0  | 24.6 |
| 3         | 5          | 78.5 | 81.3 | 9.9 | 8.8 |
| 4         | 6          | 86.4 | 85.7 | 10.4 | 3.9 |
| 5         | 7          | 93.2 | 89.2 | 10.2 | 0.6 |
| 6         | 8          | 93.0 | 90.1 | 9.3  | 0.6 |
| 7         | 9          | 93.4 | 88.6 | 10.3 | 1.1 |

Note: Reaction conditions: p-cresol, 5 mmol; TBA, 5 mmol; BAIL-2, 5 mmol; cyclohexane, 3 mL; reaction temperature, 70°C.
the selectivity of 2-TBC was also discussed (Table 5). With the amount of BAILs increasing, the conversion of \( p \)-cresol and the selectivity of 2-TBC both increase. When the molar ratio of BAILs/\( p \)-cresol is equal to 1, the selectivity of 2,6-DTBC improves gradually. When the amount of BAILs increase, the acidity of reaction mixture improve, which led to the conversion of \( p \)-cresol increase. When the molar ratio of BAILs to \( p \)-cresol is more than 1, the excessive strong acidic BAILs-1 and 2 might accelerate the reaction of 2-TBC with TBA and generate dialkylated products.

The recoverability and recyclability of BAIL-2 were also investigated. Upon completion, BAIL-2 was reused after extracted with diethyl ether and then dried under vacuum. The recycle test results were listed in Table 6. A slight decrease in conversion and a slight increase in selectivity of 2-TBC were observed after BAIL-2 were reused for five times. For recovered BAIL-2, the characteristic IR bands for organic cations are well reserved. But compared to fresh ionic liquids, there is a slight decrease in Hammet acidity function. This observation may account for slight decrease of conversion and increase of selectivity. A possible reason for the slight deactivation of BAIL-2 might be ascribed to the slight degradation of organic cation during the regeneration.

Based on this success, the alkylation of phenol with TBA was also investigated. The results were listed in Table 7. Compared to single \( \text{SO}_3\text{H} \)-functionalized BAILs-3 and -5, BAILs-1 and 2 both gave the highest conversion of phenol and selectivity of 2,4-DTBP. This can be attributed to the following facts: (1) BAILs-1 and -2 provided a stronger acidic environment, which is beneficial for 2-TBP, and 4-TBP continued to react with TBA and gave dialkylated products and (2) the steric hindrance of 2,6-DTBP.

### Experimental
All chemicals were of analytical grade and were used as received. \(^1\)H NMR and \(^{13}\)C NMR spectra were recorded on a Bruker 400 spectrometer at ambient temperature in \( \text{D}_2\text{O} \) using TMS as internal standard. Elemental analyses (C, H, N) were performed on a CHN elemental analyzer (FlashEA1112). FT-IR spectra were recorded by a Perkin-Elmer FT-IR 240-c spectrophotometer using liquid film. TG analysis was carried out with a STA409 instrument in dry air at a heating rate of 10°C/min.

### Preparations of double \( \text{SO}_3\text{H} \)-functionalized long-chain BAILs-1 and -2
BAILs-1 and 2 were synthesized according to previous literatures (20, 21). For the synthesis of BAILs-1, tetramethylethylene diamine (0.1 mol) and 1,3-propylene sulfonate (0.21 mol) were dissolved in \( \text{CH}_3\text{CN} \) (30 mL) and stirred at room temperature for 24 h. On completion, the obtained white solid was filtered off. It was washed with diethyl ether three times and dried under vacuum at 70°C for 8 h to give the zwitterions with the yield of 95\%. After the obtained zwitterions were dissolved completely in deionized water, a stoichiometric amount of \( \text{H}_2\text{SO}_4 \) was added.
in drop-wise within 1 h under vigorous stirring. Then the mixture was heated to 60°C and reacted for 8 h. After the removal of water under vacuum, BAIL-1 was obtained with a yield of 95%. 1H NMR (400 MHz, D2O) δ = 2.256–2.298 (m, 4H, 2CH3), 2.987–3.031 (t, J = 4.0Hz, 4H, 2CH2), 3.272(s, 12H, 4CH3), 3.594–3.636 (t, J = 4.4Hz, 4H, 2CH2), 3.980 (s, 4H, 2CH2); 13 C NMR (100MHz, D2O) δ = 31.83, 47.86, 50.81, 63.33, 64.17; Anal. Calcd. for C12H32N2 O14S4: C 25.35, H 5.67, N 5.91, S 22.55; Found: C 25.32, H 5.79, N 5.03, S 23.04; FT-IR: 3435, 2945, 2857,1645, 1493, 1182,1046, 800, 610 cm−1. The decomposition temperature of BAIL-1 was about 523 K.

BAIL-2 was obtained with yield of 91%. 1H NMR (400MHz, D2O) δ = 2.160–2.220 (m, 4H, 2CH2), 2.238 (s, 3H, CH3), 2.934–2.969 (m, 8H, 4CH2), 3.130 (s, 12H, 4CH3), 3.471–3.515 (m, 8H, 4CH2); 13 C NMR (100 MHz, D2O) δ = 32.13, 48.14, 51.09, 63.67; 64.04, 64.56; Anal. Calcd. for C15H40N3O18S5:C 25.89, H 5.79, N 5.03, S 23.04; Found: C 25.85, H 5.77, N 4.96, S 22.98; FT-IR:3435, 2976, 2871,1470, 1186, 1042, 793, 610 cm

General procedures of alkylation reaction

The alkylation of p-cresol or phenol with TBA was carried out in a glass reactor equipped with a magnetic stirrer. Typically, 5 mmol ionic liquids, 5 mmol p-cresol or phenol, 5 mmol TBA, and 3 mL cyclohexane were added; the mixture was stirred vigorously at 70°C for 7 h. The products were analyzed with GC equipped with a capillary column (30 m×0.25 mm×0.3 μm) and a flame ionization detector. The concentration of the reactants and the products was directly given by the system of GC chemstation according to the area of chromatography peak.

Conclusion

Two novel long-chain double SO3H-functionalized BAILs-1 and 2 were prepared using commercial available aliphatic diamine and triamine as starting materials via two-step atom economic reaction. They served as efficient and recyclable catalyst realized selective alkylation of p-cresol and phenol with TBA under mild conditions. BAIL-2 can be reused for five times after simple treatments without significant loss in conversion and selectivity.

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