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Article

An Efficient and Mild Method for the Alkylation of p-Cresol with tert-Butyl Alcohol

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Abstract: The synthesis 2-tert-butyl-4-methylphenol is of great significance because of its widely application in industry, and the development of highly efficient catalyst is necessary to the alkylation of p-cresol and tert-butyl alcohol. Here, an efficient and mild method was established, caprolactam was chosen as hydrogen-bonding acceptor, p-toluenesulfonic acid was employed as hydrogen-bonding donor, and deep eutectic solvent (DES) was prepared to catalyze the alkylation reaction. The structure of the deep eutectic solvent catalyst was characterized by ^{1}H NMR spectra, thermogravimetric analysis and fourier transform infrared spectra (FT-IR). In addition, response surface design based on Box-Behnken method was employed to optimize the alkylation reaction process parameters, the study of reaction kinetics was also carried out subsequently. The recycle performance of the catalyst was evaluated by recovery experiments, and a good result was obtained. Comparing with the literature reported, we here provide a mild method to the synthesis of 2-tert-butyl-4-methylphenol.

Keywords: Alkylation reaction; deep eutectic solvent; mild; response surface methodology

1. Introduction

The efficient synthesis of 2-tert-butyl-4-methylphenol (2-TBM) is an important reaction, because of its great application in the preparation of many kinds of fine chemicals, additive in food industry, UV-absorber and polymerization inhibitor [1-4]. Although many synthesis methods have been developed, the alkylation of p-cresol and tert-butyl alcohol to synthesis 2-TBM has been proved to be the most effective way because of the convenient operation in the reaction process. Catalyst is of great importance for the alkylation of p-cresol and tert-butyl alcohol to synthesis 2-TBM, an efficient catalyst can reduce the reaction energy barrier, and much milder reaction conditions can be used in reaction system. According to the literature reported, both heterogeneous and homogeneous catalysts for the preparation of 2-TBM have been reported, however, these catalyst systems are least preferred since they generate many problems such as corrosion, environmental safety, catalyst recyclability and so on [5-8]. Hence, the eco-friendly and commercially viable catalyst systems are still in demand for alkylation reaction to synthesis 2-TBM.

Over the past few decades, an increasing interest has been focused on developing eco-friendly catalyst system, and deep eutectic solvent has attracted much attention because of its advantages such as environment friendly, easy to synthesis, high thermal stabilities, low vapor pressures, low volatility and low cost [9-15]. As early as 2002, Abbott et al found that the mixtures of quaternary ammonium salts with amides can form low melting point eutectics, and the unusual solvents strongly influenced by hydrogen bonds [16]. Deep eutectic solvent has been wildly applied in extraction of biomass, absorption of acidic gas, organic synthesis and other fields [17-20]. Particularly, different kinds of deep eutectic solvents have been used as catalyst in esterification [21-24], oxidation [25-27] and alkylation reaction [28, 29] successfully. The application of deep eutectic solvents widely in chemical reaction gives a green and efficient choice for the catalytic reaction. However, as far as we know, there is still no literature reported on the application of deep eutectic solvent in alkylation of p-cresol and tert-butyl alcohol to prepare 2-TBM. Here, the alkylation reaction catalyzed by deep eutectic solvent was investigated, response surface design based on Box-Behnken method was employed to optimize the alkylation reaction process parameters, the study of reaction kinetics was also carried out subsequently. A method for the alkylation of p-cresol and tert-butyl alcohol was developed, which may provide an efficient and mild way to the synthesis of 2-TBM in industry.

2. Results and Discussion

2.1. Structure characterization of CAL-TsOH

2.1.1. H NMR analysis for CAL-TsOH

In order to characterize the catalyst, ^{1}H NMR characterization of caprolactam, p-toluenesulfonic acid and CAL-TsOH were employed firstly in our experiments, the results were showed in Figure 1. For the pure p-toluenesulfonic acid, the chemical shifts of aromatic ring were 7.47 and 7.10 ppm, however, the chemical shifts of aromatic ring move to 7.59 and 7.25 ppm respectively, which indicated the formation of hydrogen bonds in CAL-TsOH.

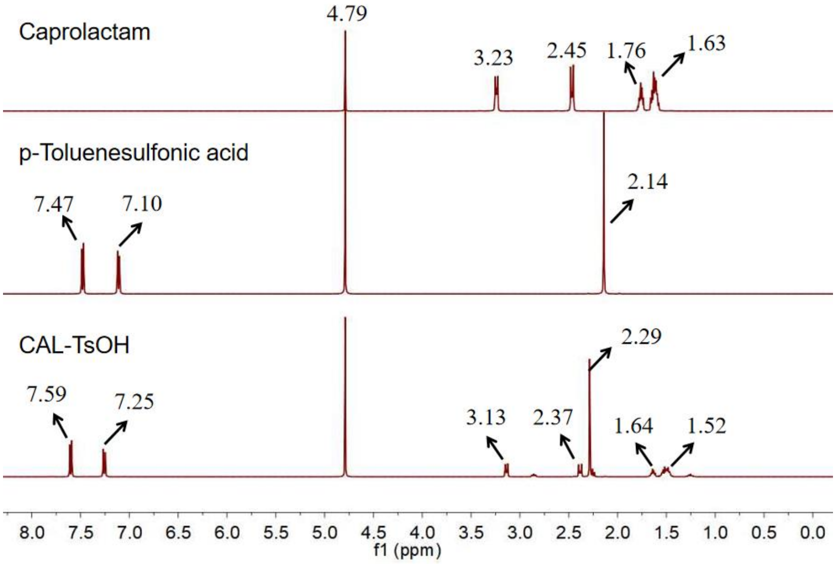


Figure 1. ^{1}H NMR of CAL-TsOH.

2.1.2. FT-IR spectra analysis for CAL-TsOH

FT-IR spectra for CAL-TsOH was determined, the adsorption bands at 3413.3 and 3035.4 cm^{-1} in Figure 2 were the stretching vibration of O-H and N-H, the hydrogen bonds in deep eutectic solvent CAL-TsOH lead to the broad adsorption peak. The peak appeared at 2946.7 and 2875.3 cm^{-1} were assigned to the stretching vibration of CH_3 and CH_2 respectively. In addition, the characteristic peaks at 1677.7 and 1496.4 cm^{-1} were assigned to the skeleton vibration of benzene ring.

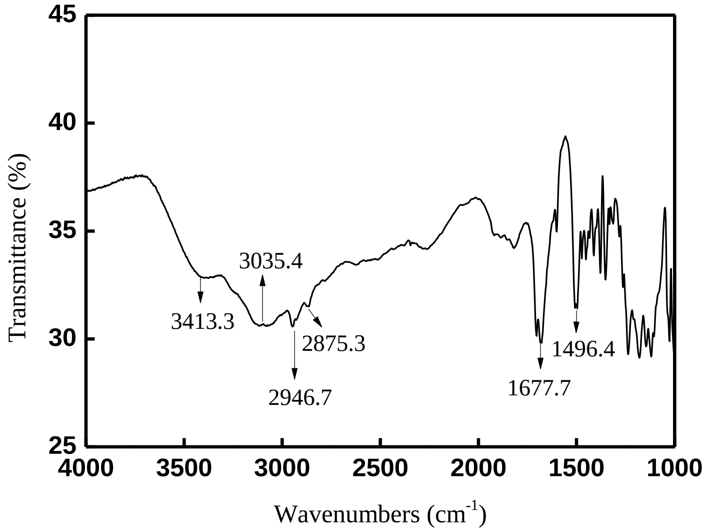


Figure 2. FT-IR spectra of CAL-TsOH.

2.1.3. Thermogravimetric analysis for CAL-TsOH

Thermogravimetric analysis was also determined for CAL-TsOH, the results were showed in Figure 3. 5.7% of mass loss of the CAL-TsOH was obtained at 120℃, which owe to the evaporation of little water in deep eutectic solvent. After that, a gentle first, then sharp decomposition process occurred in TG curve of CAL-TsOH. The decomposition temperature was found as 180℃, which indicated the good thermostability of CAL-TsOH.

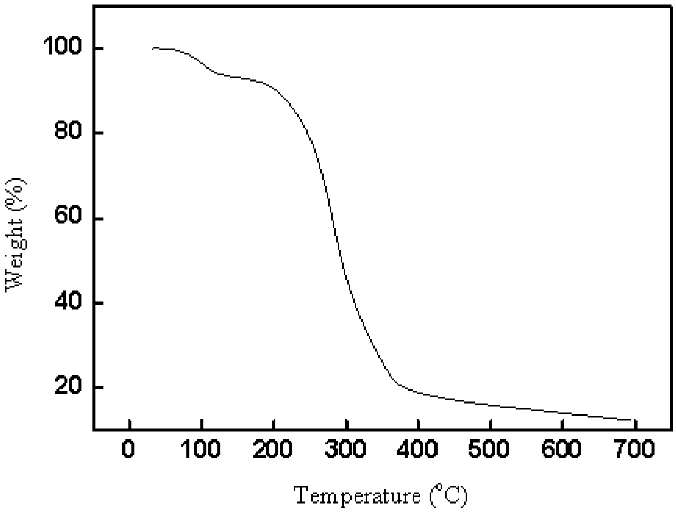


Figure 3. TG curve of CAL-TsOH.

2.2. Optimization of the conditions for the synthesis of 2-TBM

2.2.1. Effect of mole ratio (p-cresol: tert-butyl alcohol) on the conversion of tert-butyl alcohol

The effect of mole ratio on the conversion of tert-butyl alcohol was explored firstly. 5 mmol tert-butyl alcohol and 20 mol% (based on the amount of tert-butyl alcohol) CAL-TsOH were used, the reaction was performed at room temperature for 10 hours, the results were showed in Figure 4. The results indicated the mole ratio of p-cresol and tert-butyl alcohol has a significant influence on the synthesis of 2-TBM, only 13% conversion was obtained when the mole ratio was set as 2, the conversion of tert-butyl alcohol increased with the increase of mole ratio of p-cresol and tert-butyl alcohol, 78% conversion was got when the mole ratio was set as 10, and 10 of mole ratio was used in the following experiments.

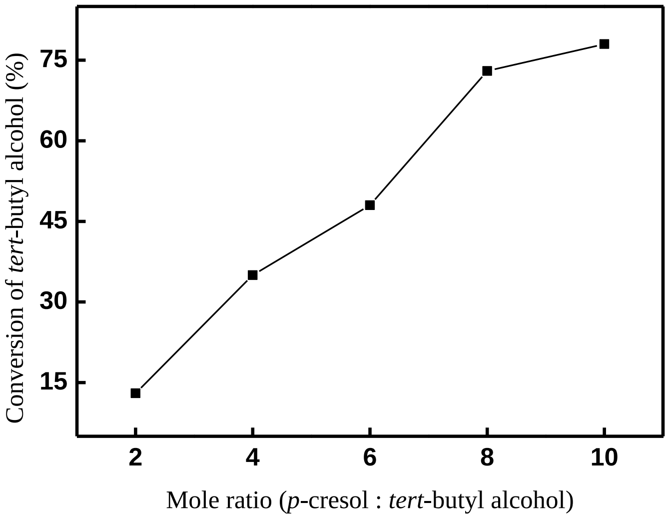


Figure 4. Effect of mole ratio on the conversion of tert-butyl alcohol.

2.2.2. Effect of dosage of catalyst on conversion of tert-butyl alcohol

The effect of dosage of CAL-TsOH on the synthesis of 2-TBM was investigated, 5 mmol tert-butyl alcohol and 50 mmol p-cresol were used in reaction system, the alkylation reaction was performed at room temperature for 10 hours, the results were showed in Figure 5. The results indicated that the conversion of tert-butyl alcohol was significantly affected by the dosage of catalyst, only 24% of conversion was obtained when the dosage of catalyst was 5 mol% (based on the amount of tert-butyl alcohol), and the conversion of tert-butyl alcohol increased with the increase of dosage of catalyst, these was no obvious increase of conversion in the synthesis reaction of 2-TBM after the dosage of catalyst increased to 20 mol%. In consideration of the economic performance, 20 mol% of CAL-TsOH was used in our following experiments.

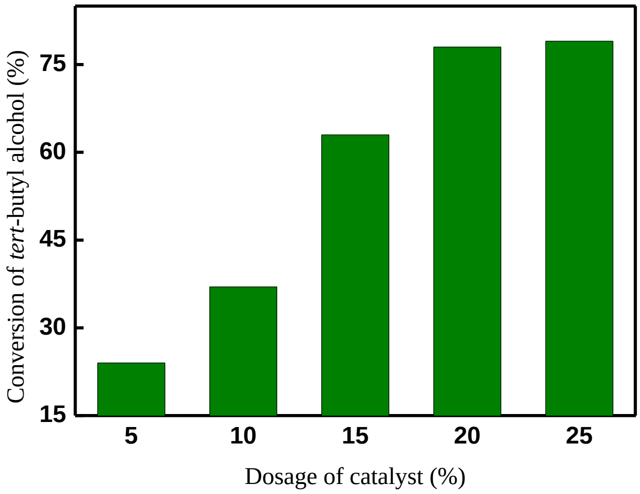


Figure 5. Effect of dosage of catalyst on conversion of tert-butyl alcohol.

2.2.3. Effect of reaction time on the conversion of tert-butyl alcohol

5 mmol tert-butyl alcohol, 50 mmol p-cresol and 20 mol% of catalyst were used in reaction system, the effect of reaction time on the synthesis of 2-TBM at room temperature was explored in our experiments, the results were showed in Figure 6. The results implied that the synthesis of 2-TBM was significantly affected by reaction time. Only 16% of conversion was obtained after reacting for 1 hours, and the conversion of tert-butyl alcohol increased quickly in the next 5 hours, 53% of conversion was got after 6 hours for the reaction time, then the conversion of tert-butyl alcohol increased slowly, although there was still a little increase when the reaction time was 12 hours, 10 hours of reaction time was more suitable, and 78% conversion of tert-butyl alcohol was obtained.

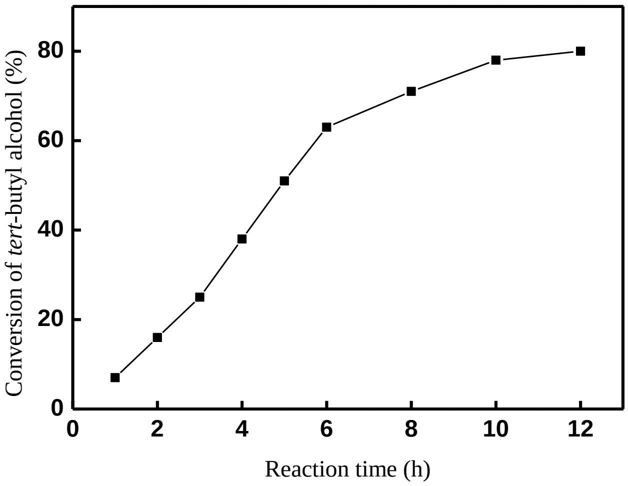


Figure 6. Effect of reaction time on conversion of tert-butyl alcohol.

2.3. Response surface methodology for the alkylation of p-cresol and tert-butyl alcohol

In this study, three main variables were mole ratio (A), dosage of catalyst (B) and reaction time (C) respectively, response factor of conversion of tert-butyl alcohol was optimized by response surface methodology. According to the results of single factor experiments, three levels of mole ratio were set as 8, 10 and 12, three levels of dosage of catalyst were set as 15, 20 and 25, then three levels of reaction time were set as 8, 10 and 12 respectively. 17 groups of experiments were designed by response surface methodology. The experimental design based on Box-Behnken design method and results were showed in Table 1, the established model for the conversion of tert-butyl alcohol was listed as follow:

$$Conversion(\%) = 78 + 2.25A + 5.88B + 2.38C + 0.25AB + 0.75AC \\ + 3.00BC - 3.50A^2 - 5.25B^2 - 1.75C^2 \quad (1)$$

Table 1. Experimental design and results of Response surface methodology.

Entry	Mole ratio	Dosage of catalyst/mol%	Reaction time/h	Conversion/%
1	10	20	10	78
2	10	15	8	68
3	10	25	12	80
4	12	25	10	79
5	10	25	8	71
6	8	15	10	60
7	10	20	10	78

8	12	20	12	79
9	8	20	8	68
10	10	20	10	78
11	8	25	10	74
12	8	20	12	73
13	12	15	10	64
14	10	20	10	78
15	10	15	12	65
16	12	20	8	71
17	10	20	10	78

To investigate the goodness of the fit for the model, analysis of variance (ANOVA) was used in our research. The results for analysis of variance were illustrated in Table 2. 0.0003 and 0.1346 of P-values for the model and lack of fit were obtained respectively, which indicated the model in equation (1) was highly significant, and the established model fitted well in the current research [30].

In order to investigate the interaction influence of mole ratio (A), dosage of catalyst (B) and reaction time (C), the 3D response surfaces were employed in Figure 7. The obvious interaction influence among mole ratio (A), dosage of catalyst (B) and reaction time (C) were found in our research because of the oval shapes of the contour lines. Subsequently, the optimization process was performed by Design-Expert, 83% conversion of tert-butyl alcohol was obtained with 10.97 of mole ratio, 24.17 mol% of dosage of catalyst and 12.00 hours of reaction time. To verify the optimization results by response surface methodology, a experiment was performed with 11 of mole ratio, 25 mol% of dosage of catalyst and 12.00 hours of reaction time, 85% conversion of tert-butyl alcohol was obtained, the results indicated the reliability of the optimization results by response surface methodology.

Table 2. Analysis of variance.

Source	**Sum of squares**	**df**	**Mean square**	**F-value**	**P-value**	
Model	597.69	9	66.41	21.88	0.0003	significant
A-mole ratio	40.5	1	40.5	13.34	0.0082	
B-dosage of catalyst	276.13	1	276.13	90.96	<0.0001	
C-reaction time	45.13	1	45.13	14.86	0.0062	
AB	0.25	1	0.25	0.082	0.7824	
AC	2.25	1	2.25	0.74	0.4178	
BC	36.00	1	36.00	11.86	0.0108	
A^2	51.58	1	51.58	16.99	0.0044	
B^2	116.05	1	116.05	38.23	0.0005	
C^2	12.89	1	12.89	4.25	0.0783	
Residual	21.25	7	3.04			
Lack of Fit	21.25	3	7.08	7.43	0.1346	not significant
Pure Error	0.00	4	0.00			

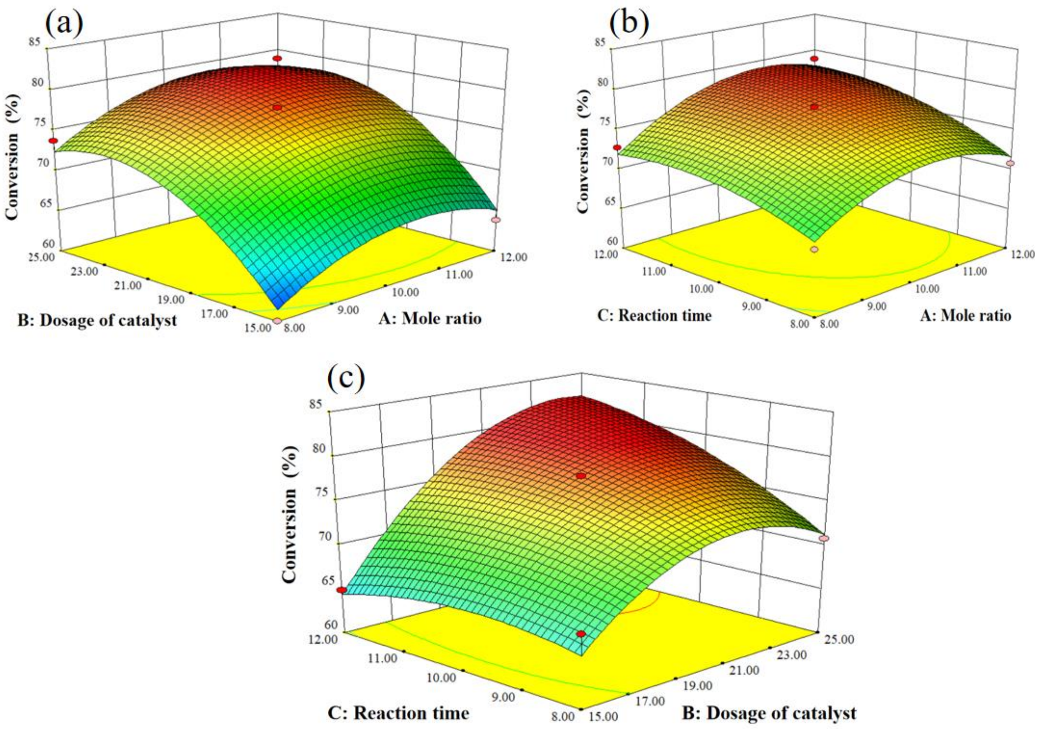


Figure 7. 3D response surface curves for the synthesis of 2-TBM: (a) dosage of catalyst and mole ratio, (b) reaction time and mole ratio, (c) reaction time and dosage of catalyst.

2.4. Comparison of CAL-TsOH with other catalysts

To thoroughly compare the potential of different catalysts for the synthesis of 2-TBM, the reaction temperature and conversion reported in the literature were summarized in Table 3. Both heterogeneous and homogeneous catalysts for the preparation of 2-TBM have been reported. For example, Elavarasanit et al. reported the alkylation of p-cresol and tert-butyl alcohol catalyzed by ionic liquid, response surface methodology was employed to optimize the process parameters, and 89.4% conversion was obtained with 348 K of reaction temperature [31]. Some other homogeneous catalyst also used in the synthesis of 2-TBM. Density functional theory was used to develop a molecular level understanding of alkylation of p-cresol and tert-butyl alcohol catalyzed by acidic ionic liquids, 86% conversion was obtained under 343 K of reaction temperature [32]. The SO$_3$H-functionalized ionic liquids were synthesized, and the catalytic performance for the alkylation of p-cresol and tert-butyl alcohol was evaluated, 79% of conversion and 92% of selectivity were obtained [33]. Kishore et al reported some novel Bronsted acidic ionic liquids, N-methyl imidazole, pyridine, triethylamine and 1,4-butanesultone was used as the source chemicals, 80% conversion was obtained under 70°C of reaction temperature [34]. In addition, the alkylation of p-cresol and tert-butyl alcohol to 2-TBC catalyzed by multiple-SO$_3$H functional ionic liquid was reported by Bao et al, 85.3% of conversion and 95.2% of selectivity were obtained [35]. Heterogeneous catalyst were also reported widely in literature, however, much higher reaction temperature was needed. WOx/ZrO$_2$ was prepared by wet impregnation method, zirconium oxyhydroxide and ammonium metatungstate were used, the catalyst 15% WO$_3$/ZrO$_2$ calcined at 800 °C found to be the most active in the reaction, 69.8% of conversion and 92.4% selectivity of 2-tert-butyl-p-cresol were obtained under the optimized reaction conditions of 130°C, tert-butanol/p-cresol molar ratio of 3 and flow rate of 10 ml h^{-1} [36]. Devassy et al reported a 12-tungstophosphoric acid supported on zirconia (TPA/ZrO$_2$) under flow conditions, the effects molar ratio of p-cresol and tert-butyl alcohol, reaction temperature and space velocity on the conversion of p-cresol and products selectivities were optimized, 61% conversion of p-cresol and 81.4 selectivity of 2-tert-butyl-p-cresol were obtained under 403 K of reaction temperature [37]. In addition, titania modified with 12-tungstophosphoric acid (TPA/TiO$_2$) catalyst was prepared by Kumbar et al, surface area, XRD, ^{31}P MAS NMR, XPS, NH_3-TPD, and FTIR pyridine adsorption were employed to characterize these catalysts, 82% conversion of p-cresol and 89.5 selectivity of 2-tert-butyl-p-cresol were obtained under the optimized reaction conditions [38]. Long chain double SO_3H-functionalized Brønsted acidic ionic liquids were synthesized, and the catalytic performance for the alkylation of p-cresol was investigated, 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 by Li et al [39]. Additionally, the alkylation of p-cresol with MTBE to synthesis 2-tert-butyl-p-cresol was investigated, a mesoporous and strong acid catalyst UDCaT-1 was prepared by Yadav et al, the ratio of p-cresol and MTBE was 1:1, the reaction temperature was set as 100 °C, 45% conversion was obtained [40].

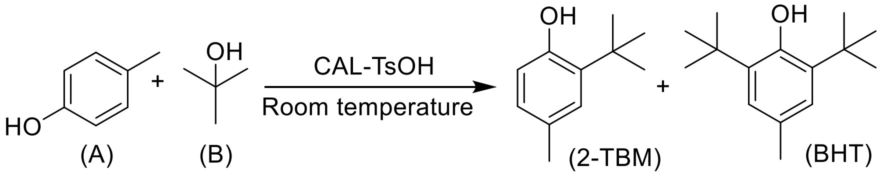
It can be clearly seen that the reaction temperature in our experiments is much milder than those catalyzed by other catalysts reported in the literature, and a satisfactory conversion of tert-butyl alcohol was obtained.

Table 3. Comparison of catalytic performance for alkylation reaction.

Entry	Catalyst	Temperature (K)	Conversion (%)	Refs
1	CAL-TsOH	298	78	This work
2	N-(1,4-sulfonic acid) butyl triethylammonium hydrogen sulfate	348	89.4	[31]
3	IL-CF_3SO_3	343	86.2	[32]
4	SO_3H ionic liquids	343	79	[33]
5	SO_3H-functionalized Bronsted acidic ionic liquid	343	80	[34]
6	mutipule-SO_3H ionic liquid	343	85.3	[35]
7	WO_x/ZrO_2	403	69.8	[36]
8	TPA/ZrO_2	403	61	[37]
9	TPA/TiO_2	403	82	[38]
10	BAIL-1	343	93.2	[39]
11	UDCaT-1	373	45	[40]

2.5. Reaction kinetics for the alkylation of p-cresol and tert-butyl alcohol

In consideration of the application for the synthesis of 2-TBM catalyzed by CAL-TsOH in industry, the investigation of reaction kinetics for the alkylation of p-cresol and tert-butyl alcohol is essential, the reaction equation can be expressed as follow:



However, there was no butylated hydroxytoluene (BHT) was found in our reaction system, 2-tert-Butyl-4-methylphenol (2-TBM) was the only product. Hence, the kinetic studies were carried out in standard reaction conditions based on the follow assumptions: (a) the intermediate products can be neglected; (b) the reverse reaction can be ignored [41,42]. The equation of reaction rate can be expressed as follow:

$$r = kC_A C_B \quad (2)$$

The excessive p-cresol (p-cresol: tert-butyl alcohol=10) was used in our experiments, thus, the concentration of p-cresol has little influence on the alkylation reaction rate. Consequently, the kinetic rate equation for the synthesis of 2-TBM at room temperature catalyzed by CAL-TsOH can be expressed as follow:

$$r = -\frac{dC_B}{dt} = kC_B \quad (3)$$

$$C_B = C_{B0}(1-y) \quad (4)$$

where, k is the alkylation reaction rate constant, h^{-1}; C_{B0} and C_B are the concentration of tert-butyl alcohol at the beginning and end of the synthesis of 2-TBM, mol·L^{-1}; y (%) is the conversion of tert-butyl alcohol determined by GC; t is the alkylation reaction time, h.

The equation (3) can be transformed to the linearization form as:

$$-\ln(1-y) = kt \quad (5)$$

Therefore, the reaction rate constant k can be calculated by plot of -ln(1-y) versus t, the fitted results of kinetic study at room temperature were showed in Figure 8, the linear correlation of R_2 was 0.975, which indicated the goodness of fit for the alkylation of tert-butyl alcohol and p-cresol, 0.18537 h^{-1} of k was obtained, hence, the kinetic equation for the alkylation of tert-butyl alcohol and p-cresol under room temperature was obtained as -ln(1-y) = 0.18537t - 0.1708. The kinetic study would be played an important role in the industrialization application for the synthesis of 2-TBM under room temperature.

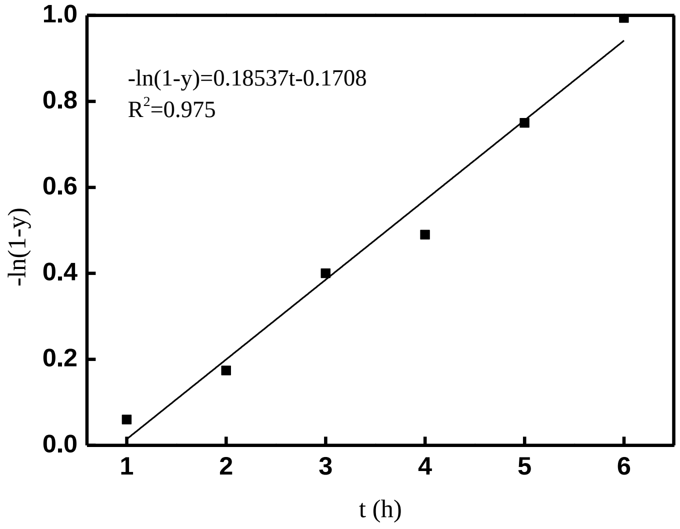


Figure 8. Fitting curve of -ln(1-y) and t.

2.6. Catalyst recovery for the CAL-TsOH

The recycle performance of the CAL-TsOH was investigated by recovery experiment. Firstly, tert-butyl alcohol, p-cresol and CAL-TsOH were mixed in a 25 mL reaction tube, a homogeneous solution was obtained, then the alkylation reaction was performed in the standard reaction condition. After the reaction, the catalyst in reaction tube was extracted by ethyl acetate, and CAL-TsOH was obtained in the lower layer. The recycled CAL-TsOH was washed by ethyl acetate for several times and dried for 24 hours at 70℃. The results of the catalyst recovery experiment were displayed in Figure 9. The conversion of tert-butyl alcohol decreased gradually after five catalytic cycles and 68% conversion was obtained, which may due to the loss of CAL-TsOH during the extract process by ethyl acetate.

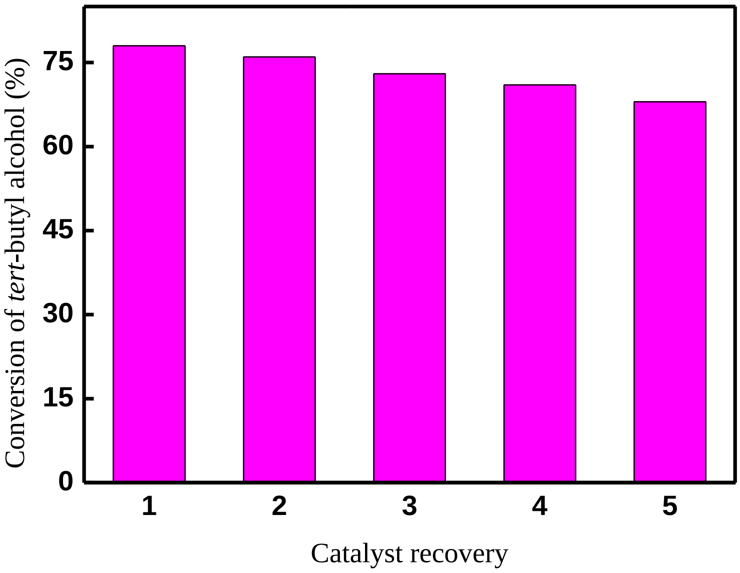


Figure 9. Results of recovery experiment for the CAL-TsOH.

3. Materials and Methods

3.1. Materials and chemicals

Caprolactam and tert-butyl alcohol were obtained from Sinopharm Chemical Reagent Co., Ltd; p-toluenesulfonic acid (TsOH) was purchased from Aladdin Reagent Co., Ltd; p-cresol was purchased from Energy Chemical Reagent Co., Ltd; ethyl acetate was purchased from Nanjing Chemical Reagent Co., Ltd. All of the reagents in this research were used without further purification.

3.2. Preparation of CAL-TsOH

Caprolactam was chosen as hydrogen-bonding acceptor, p-toluenesulfonic acid was employed as hydrogen-bonding donor. 3.44 g p-toluenesulfonic acid and 2.26 g caprolactam were mixed and stirred at 80℃ for 24 hours in a 25 mL round-bottomed flask. Then, a homogeneous and clear liquid of CAL-TsOH was obtained.

3.3. Characterization of CAL-TsOH

Bruker Avance 400 spectrometer was employed to record ^1H NMR of CAL-TsOH, D_2O was used as solvent. FT-IR spectra of CAL-TsOH was obtained by Nicolet iS50 spectrometer. In order to investigate the thermostability of the catalyst, thermogravimetric analysis (TGA) was performed under N_2 atmosphere, the heat rate was set as 10℃/min from 30 to 700℃.

3.4. Procedure for the synthesis of 2-TBM

50 mmol p-cresol and 5 mmol tert-butyl alcohol were mixed in a 25 mL reaction tube, 20 mol% (based on the amount of tert-butyl alcohol) of CAL-TsOH was used. The reaction tube was put into a parallel apparatus which equipped with condensation unit subsequently. The reaction tube was stirred for 10 hours at room temperature subsequently. Then, the CAL-TsOH catalyst in reaction tube was extracted by ethyl acetate, gas chromatography was used to determine the conversion of tert-butyl alcohol.

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3.5. Single factor experiments

3.5.1. Effect of mole ratio on the conversion of tert-butyl alcohol

The effect of mole ratio on the conversion of tert-butyl alcohol was performed firstly. 5 mmol tert-butyl alcohol and 20 mol% CAL-TsOH were used in our reaction system, the reaction was performed at room temperature for 10 hours, the mole ratio of p-cresol to tert-butyl alcohol was set as 2, 4, 6, 8 and 10 respectively. The conversion of tert-butyl alcohol was determined by GC to investigate the effect of mole ratio.

3.5.2. Effect of dosage of catalyst on the conversion of tert-butyl alcohol

The effect of dosage of catalys on the conversion of tert-butyl alcohol was investigated. 5 mmol tert-butyl alcohol and 50 mmol p-cresol was used, the dosage of catalyst was set as 5, 10, 15, 20 and 25 mol% CAL-TsOH (based on tert-butyl alcohol) respectively in our reaction system, the reaction was performed at room temperature for 10 hours. After the reaction, the conversion of tert-butyl alcohol was determined by GC to investigate the effect of dosage of catalyst.

3.5.3. Effect of reaction time on the conversion of tert-butyl alcohol

The effect of reaction time on the conversion of tert-butyl alcohol was investigated. 5 mmol tert-butyl alcohol, 50 mmol p-cresol and 20 mol% of catalyst were used, the effect of reaction time on the synthesis of 2-TBM at room temperature was investigated in our reaction system. After the reaction, the conversion of tert-butyl alcohol was determined by GC to investigate the effect of reaction time.

3.6. Experimental design of response surface methodology

In order to investigate the interaction influence of mole ratio (A), dosage of catalyst (B) and reaction time (C), response surface methodology was used in our experiment. According to the results of single factor experiments, a three factors and three levels experiments were designed based on Box-Behnken method. The conversion of tert-butyl alcohol was set as response value, and the synthesis of 2-TBM process was optimized by response surface methodology.

3.6. Determination of the conversion of tert-butyl alcohol

Shimadzu GC 2014C was employed to determine the conversion of tert-butyl alcohol, FID detector and RTX-5 capillary column were equipped. The temperatures of FID detector and gasification chamber were set as 300℃, the temperature of the column was 40℃ initially and held for 2 min, then the column was programmed to heat up until 280℃ at a heat rate of 30℃/min and held for 3 min. In addition, the conversion of tert-butyl alcohol was calculated according to the the determination results by GC. The calculated equation can be expressed as follow:

$$Conversion = \frac{n_{B0} - n_B}{n_{B0}} \times 100\% \qquad (6)$$

n_{B0} and n_B are the mole numbers of tert-butyl alcohol at the beginning and end of the synthesis of 2-TBM.

4. Conclusions

An efficient and mild method was established, caprolactam was chosen as hydrogen-bonding acceptor, p-toluenesulfonic acid was employed as hydrogen-bonding donor, and deep eutectic solvent was prepared to catalyze the alkylation reaction of p-cresol and tert-butyl alcohol. ^{1}H NMR spectra, thermogravimetric analysis and FT-IR spectra were performed to characterize the CAL-TsOH. Response surface methodology was employed to optimize the conditions for the preparation of 2-TBM, 83% conversion of tert-butyl alcohol was obtained with 10.97 of mole ratio, 24.17 mol% of dosage of catalyst and 12.00 hours of reaction time. In addition, the reaction kinetics, and 0.18537 h^{-1} of reaction rate constant k was obtained. The recovery experiment was also used to evaluate the recycle performance, the conversion decreased gradually after five catalytic cycles and 68% conversion was obtained. Comparing with other reports, it can be clearly seen that the reaction temperature in our experiments is much milder than those catalyzed by other catalysts reported, and a satisfactory conversion of tert-butyl alcohol was obtained. The method provideep eutectic solventa mild way for the synthesis of 2-TBM in industry.

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Conflicts of Interest: The authors declare no conflict of interest.

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