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ESTERIFICATION OF SALICYLIC ACID USING Ce^{4+} MODIFIED CATION-EXCHANGE RESIN AS CATALYST

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ABSTRACT

The esterification of salicylic acid with methanol was carried out over a series of Ce^{4+} modified cation-exchange resins. The effect of different reaction conditions was studied on the conversion of salicylic acid, and the optimal reaction parameters were obtained. The experimental results indicated that $Ce(SO_4)_2$/001×7 was an effective catalyst for the synthesis of methyl salicylate. The conversion of salicylic acid could reach 93.3% while its selectivity was more than 99.0%. SEM-EDS and TG-DSC analysis were employed to characterize the structure and property of the catalyst. Besides, the catalytic performance of $Ce(SO_4)_2$/001×7 in the esterification of salicylic acid with different alcohols was compared. The reusability of $Ce(SO_4)_2$/001×7 was also studied by using salicylic acid and methanol as model substrates. The mechanism was proposed for the esterification of salicylic acid with methanol over Ce^{4+} modified cation-exchange resins.

Keywords: Salicylic acid, Esterification, Metal modified, Cation-exchange resin

INTRODUCTION

Organic esters which represent peculiarly medicinal and chemical characteristics have been extensively used in the synthesis of drugs, plasticizers, food preservatives, pharmaceuticals, solvents, perfumes, cosmetics, and chiral auxiliaries[1]. Conventional mineral catalysts for esterification reaction included H_2SO_4, HF, H_3PO_4, $NaHSO_4$ and so on. However, these catalysts often suffered from inherent problems of corrosiveness, more byproducts, environmental hazards, difficulty in catalyst recovery and reuse, susceptibility to water[2]. A variety of materials such as clays, zeolites, mesoporous materials, sulfated metal oxides and heteropolyacids have been developed as solid acid catalysts in esterification reactions[3, 4]. In esterification reactions, their main advantages in comparison to conventional mineral catalysts were non-corrosive and easy to be separated from the reaction mixture for reuse[5]. However, these catalysts had their own shortcomings such as the hybrid acid sites and deconcentrated acidity, leading to low selectivity toward target product[6]. To solve these problems, ionic liquids (ILs) have been explored as a new green reaction media owing to their negligible volatility, excellent thermal stability, and the variety of structures available[7-9]. Hence, studies about ILs in esterification were hot[10-13]. However, the high cost restricted the application of ILs in esterification industry.

Ion-exchange resins, which have a bead structure, the advantages of solid acid catalysts, and the ability to ion-exchange or chelate metal ions, have been widely applied in many fields, such as purification of water and wastewater, separation of heavy metal ions, esterification and etherification reactions[14-18]. Besides, Yonemoto[19] and Li[20] have reported on the biodiesel production using anion-exchange and cation-exchange resins as heterogeneous catalysts respectively. Furthermore, several references in the form of research articles were available on the application of metal-doped resins. Arnold[21], Drelinkiewicz[22], and Kralik[23] reported that metal-doped resins were efficient for epoxidation, carbon–carbon coupling, hydrogenation, and hydroformylation reactions. Within the application of esterification, many studies have focused primarily on the kinetic study of cation-exchange resins catalyzed in the synthesis of various esters[24-26]. A careful survey of literature showed that there were few detailed studies about metal modified cation-exchange resins catalyzed in the esterification of salicylic acid.

In the present work, modified cation-exchange resin $Ce(SO_4)_2$/001×7 was synthesized, characterized and used in the synthesis of salicylate. The catalytic performance of $Ce(SO_4)_2$/001×7 in the esterification of salicylic acid with different alcohols was compared. The reusability of $Ce(SO_4)_2$/001×7 was also examined using salicylic acid and methanol as model substrates. An attempt was also made to study the mechanism of the esterification reaction.

EXPERIMENTAL

1. Materials

Cation-exchange resins (D001-cc, 001×7, D61, D72, NKC-9) were purchased from the Chemical Plant of Nankai University, China. These resins were pretreated using methods in the previous literature[20]. All reagents (A.R.) were purchased from China National Pharmaceutical Group Corporation (Shanghai) and treated according to standard methods.

2. Sample preparation

Modified cation-exchange resin $Ce(SO_4)_2$/001×7 was prepared as follows: 1 mL of 98 wt.% sulfuric acid was added into 20 mL of distilled water. And then under vigorous stirring, 1.22 g of $Ce(SO_4)_2 \cdot 4H_2O$ was dissolved in the above sulfuric acid solution. Finally, 4.0 g of cation-exchange resin 001×7 with pre-treatment was added and stirred for 3 h, aged for 3 d, filtered at room temperature and activated at 100ºC in a vacuum. The content of ceric sulfate in catalyst was 20%. For comparison, other Ce^{4+} modified cation-exchange resins were synthesized with the similar method.

3. Catalyst characterization

Thermogravimetric and differential scanning (TG-DSC) analysis was carried out on a Model STA-449C Jupiter apparatus (Netzsch Corporation, Selb, Germany). The testing process was 30-1000ºC at a heating rate of 10ºC/min under a N_2 atmosphere.

SEM-EDS measurements were conducted on catalysts using a field-emission scanning electron microscope (Hitachi, S-4800) equipped with an energy dispersive X-ray spectroscope (EDS) operated at an acceleration voltage of 10 kV.

4. Catalytic activity investigation

The esterification of salicylic acid (SA) with methanol was carried out as the model reaction to investigate the catalytic activity. This reaction was performed at atmospheric pressure and refluxed in a single-neck flask with a condenser. The reactor was heated in a temperature-controlled oil bath with a magnetic stirrer. In a typical procedure, the reaction substrates containing 0.01 mol of SA, some methanol and catalyst were heated for hours. After reaction, diethyl ether was added to dissolve the unreacted SA. The mixture was divided into two phases. The upper liquid phase consisting of the produced ester and some unreacted SA was separated by decantation, while the lower solid phase, the catalyst, could be reused after removal of water.

The composition of products was analyzed by gas chromatography-flame ionization detector (GC-FID) (Agilent 7890A, HP-5 column, 30 m × 0.32 mm i.d. × 0.25 μm film thickness). The GC-FID conditions were as follows: detector temperature, 300ºC; injection port temperature, 300ºC; oven temperature program, 70-170ºC at a 15ºC/min gradient; injection volume of sample, 0.4 μL. The products were identified by comparing with the standards. GC results showed that the major product was methyl salicylate and the minor side product was phenol. The conversion and selectivity were calculated according to the area of chromatograph peak using the following expressions[27]:

$$\text{Conversion of salicylic acid (SA) (\%)} = 100 - \frac{[\text{salicylic acid}]}{[\text{salicylic acid}] + [\text{methyl salicylate}] + [\text{phenol}]} \times 100 \qquad (1)$$

$$\text{Selectivity of methyl salicylate (MS) (\%)} = \frac{[\text{methyl salicylate}]}{[\text{methyl salicylate}] + [\text{phenol}]} \times 100 \qquad (2)$$

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RESULTS AND DISCUSSION

1. TG-DSC analysis

As is described in Fig. 1, TG-DSC analysis was carried out to investigate the thermal stability of $Ce(SO_4)_2$/001×7.

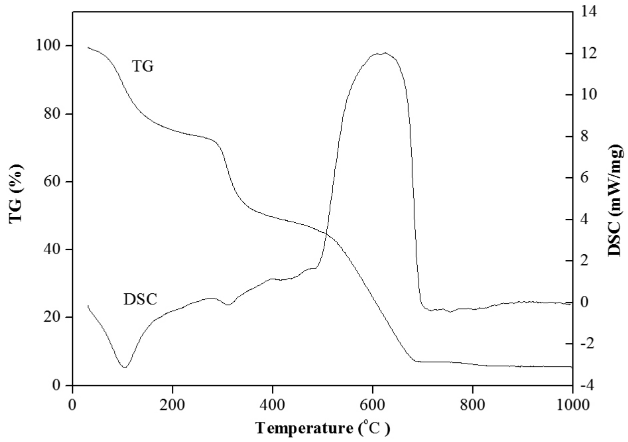
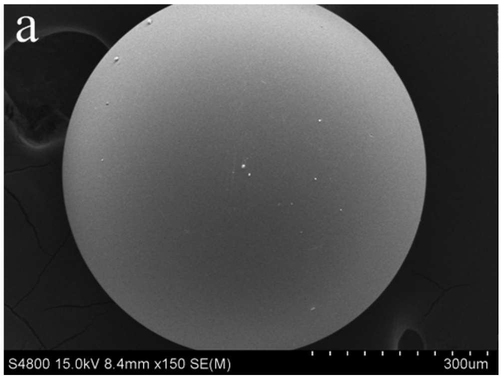


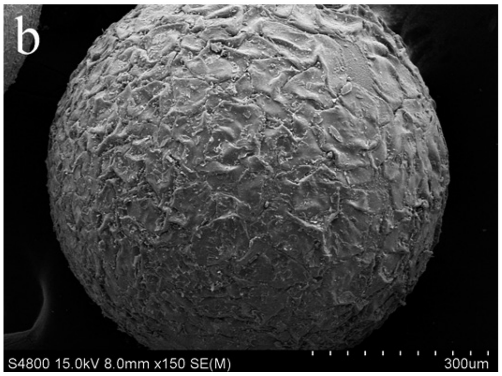
Figure 1: TG and DSC curves of $Ce(SO_4)_2$/001×7.

In the range of 30-100ºC, the weight loss may be caused by the physically absorbed water in the catalyst. From 100 to 310ºC, the weight loss may be duo to the partial carbonization of the resin. By further heating (from 310 up to 510ºC), a two step endothermic process happened. The weight loss between 310 and 420ºC may be attributed to the loss of the sulfonic groups and short alkyl groups in resin[28]. The weight from 420 to 510ºC was lost in the transformation of $Ce(SO_4)_2$ into $Ce_3O_2(SO_4)_4$ and SO_3. From 510-700ºC, the decomposition of styrene-divinylbenzene copolymer took place, and finally $Ce_3O_2(SO_4)_4$ turned into CeO_2 and SO_3[29].

2. SEM-EDS analysis

SEM photomicrographs of 001×7 and $Ce(SO_4)_2$/001×7 are presented in Fig. 2 and Fig. 3. EDS analysis is carried out on fresh $Ce(SO_4)_2$/001×7 in the SEM equipped with EDS (Fig. 3d).





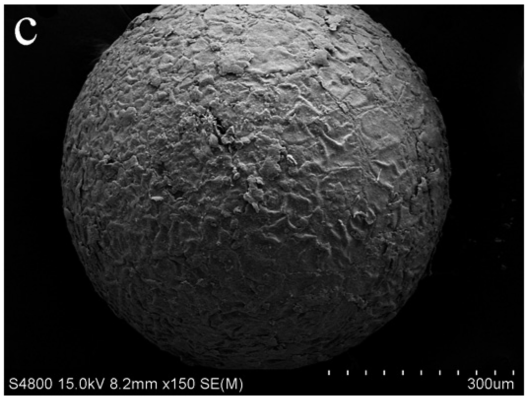
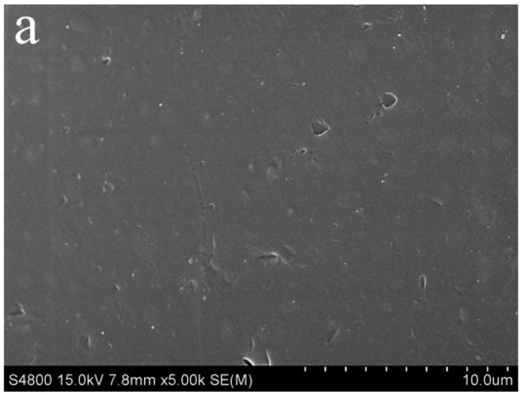
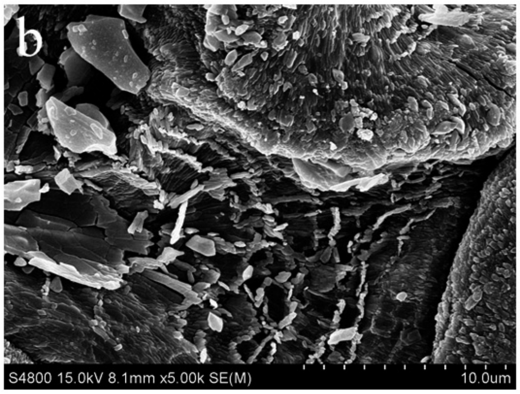
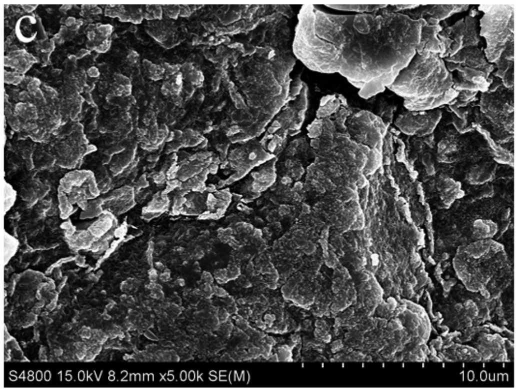


Figure 2 SEM photomicrographs of the surface of the catalysts: (a) resin 001×7, (b) fresh $Ce(SO_4)_2$/001×7 , and (c) $Ce(SO_4)_2$/001×7 after the first recycling reaction. Magnification: 150.







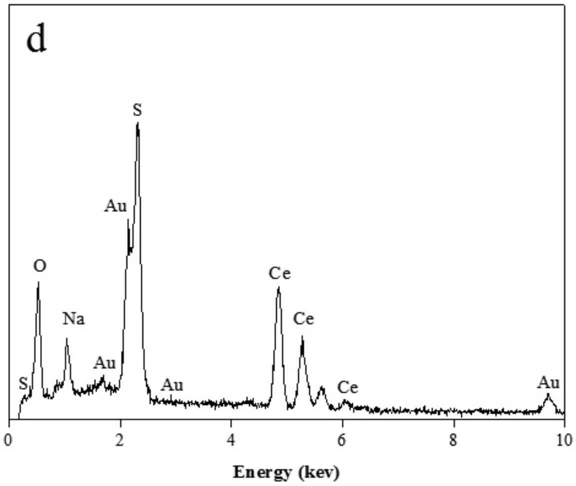


Figure 3 SEM photomicrographs of the surface of the catalysts: (a) resin 001×7, (b) fresh $Ce(SO_4)_2$/001×7, (c) $Ce(SO_4)_2$/001×7 after the first recycling reaction, and (d) EDS of fresh $Ce(SO_4)_2$/001×7. Magnification: 5000.

As is shown in Fig. 2 and Fig. 3, SEM photographs are under the magnification of 150 and 5000, respectively. In Fig. 2a, the surface of resin 001×7 was smooth like most of gel resins. After the introduction of $Ce(SO_4)_2$, the surface of $Ce(SO_4)_2$/001×7 (Fig. 2b) changed obviously in comparison to 001×7. At high magnifications, the surface of $Ce(SO_4)_2$/001×7 (Fig. 3b) was rough, whereas the surface of 001×7 (Fig. 3a) was relatively plain. Compared with Fig. 2b and Fig. 3b, Fig. 2c and Fig. 3c showed that there were no obvious changes on the surface of $Ce(SO_4)_2$/001×7 after esterification reaction. EDS analysis also indicated $Ce(SO_4)_2$ existed on the surface of the resin. The Na signal in the EDS was from the rudimental sodium ion in the resin after pre-treatment, and the Au was sprayed when preparing the sample (Fig. 3d).

3. Effect of different reaction systems

As could be indicated in Table 1, cerium sulfate was effective for the esterification of salicylic acid. It was clear that catalytic performance of the resin was obviously improved after modified with $Ce(SO_4)_2$, and $Ce(SO_4)_2$/001×7 was relatively active. With the incorporation of $Ce(SO_4)_2$, the total acid sites of the catalysts greatly increased and the catalytic activity could be effectively enhanced. Besides, the selectivity for methyl salicylate was more than 99.0%, which was closely related to the strong acid strength and the distribution of the catalyst[30]. $Ce(SO_4)_2$/001×7 was used as a typical catalyst to obtain the optimal reaction parameters for the synthesis of methyl salicylate.

Table 1: Effect of different esterification systems[a]

Entry	Type of resins	SA conversion of different esterification systems (%)		
		Modified with $Ce(SO_4)_2$	Without $Ce(SO_4)_2$	$Ce(SO_4)_2$ only
1	001×7	93.3	55.7	76.2
2	D061	90.6	48.1	
3	D001-cc	88.2	34.3	
4	D72	81.4	42.7	
5	NKC-9	83.5	52.5	

[a] Reaction conditions: molar ratio of SA to methanol, 1:3; temperature, 368 K; time, 12 h; catalyst weight, 0.4 g.

4. Optimization of reaction conditions

The esterification reaction was carried out using different molar ratios of salicylic acid (SA) to methanol varied from 1:2 to 1:6 under the same reaction condition (Fig. 4). When the molar ratio reached a critical value (1:3), the conversion of SA for the catalyst $Ce(SO_4)_2$/001×7 was up to the top level 93.3%. In the case of $Ce(SO_4)_2$/D061 and $Ce(SO_4)_2$/D001-cc, for the same molar ratio from 1:2 to 1:6, the conversion levels were lower than that of $Ce(SO_4)_2$/001×7. The selectivity for methyl salicylate in all cases remained above 99.0%.

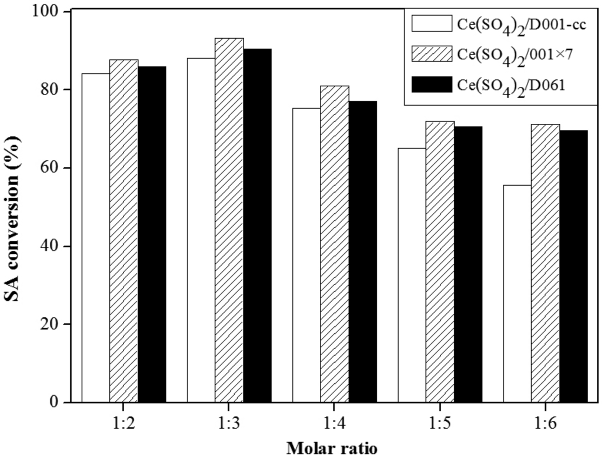


Figure 4 Esterification of salicylic acid with methanol, effect of molar ratio of salicylic acid to methanol. Reaction conditions: catalyst weight, 0.4 g; time, 12 h; temperature, 368 K.

In Fig. 5, the esterification reaction was executed with different amounts of $Ce(SO_4)_2$/001×7 under the same reaction condition. As the amount of the catalyst increased from 0.1 g to 0.5 g, the conversion of SA was improved from 46.7% to 94.1%. This could be attributed to the number of Lewis acid sites increasing as the catalyst amount increased. When the catalyst concentration exceeded 0.4 g, the increase of SA conversion was not obvious. In all cases, the selectivity for methyl salicylate was more than 99.0%.

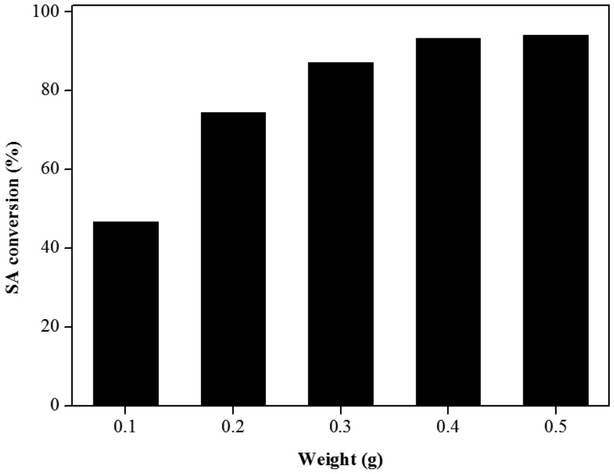


Figure 5 Esterification of salicylic acid with methanol, effect of catalyst weight. Reaction conditions: molar ratio of SA to methanol, 1:3; reaction time, 12 h; reaction temperature, 368 K.

As is shown from Fig. 6, the esterification system composed of salicylic acid (SA), methanol and the catalyst $Ce(SO_4)_2$/001×7 was used to research the influence of various reaction time and temperatures. The conversion of SA increased at different temperatures with the increase of time. For instance, the conversion of SA at 368 K increased from 75.1% to 93.3% when the reaction time was changed from 6 h to 12 h. However, the conversion of SA increased slowly to 93.8% when reaction time reached 14 h. Besides, the results displayed that the reaction activity was the best at 368 K for 12 h, and the conversion of SA could reach 93.3%. However, at 373 K and 363 K, it only got to 91.5% and 87.7%, respectively.

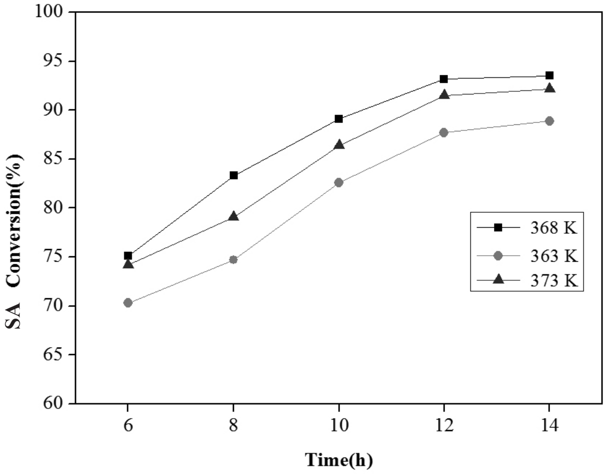


Figure 6 Esterification of salicylic acid with methanol, effect of temperature and reaction time. Reaction conditions: molar ratio of SA to methanol, 1:3; catalyst weight, 0.4 g.

From the above study, the suitable condition for the reaction could be found as follows: molar ratio of SA to methanol, 1:3; temperature, 368 K; time, 12 h; catalyst weight, 0.4 g. The selectivity for methyl salicylate in all cases remained above 99.0%.

5. Esterification of different alcohols catalyzed by $Ce(SO_4)_2$/001×7

Data in Table 2 illustrated the catalytic performance of $Ce(SO_4)_2$/001×7 in the esterification of salicylic acid with methanol and other kinds of alcohols under the same condition. For methanol, the SA conversion was the highest, 93.3%. Besides, the SA conversions for ethanol, butanol, pentanol, hexanol, and octanol were much lower, which were 71.5%, 70.6%, 46.0%, 61.3%, and 46.0%, respectively. These results showed that the SA conversion of alcohols was related to the length of carbon chain and the dielectric constant[31]. Alcohols with shorter carbon chain gave higher conversion. It was due to the increase of steric hindrance when the carbon chain grew longer. This would hinder the esterification reaction to the direction of ester formation. The dielectric constant indicated how easy a material could be polarized by imposition of an electric field on an insulating material. The dielectric constants of methanol, ethanol, butanol, pentanol, hexanol, and octanol were 33.0, 25.3, 17.8, 13.9, 13.3, and 8.1 at room temperature respectively[32]. Alcohols with higher dielectric constant gave higher SA conversion. Hence, the length of carbon chain and the dielectric constant may have synergistically effect on the esterification of salicylic acid.

Table 2 Esterification of different alcohols catalyzed by $Ce(SO_4)_2$/001×7[a]

Entry	Alcohol	Conversion (%)	Selectivity (%)[b]
1	Methanol	93.3	99.9
2	Ethanol	71.5	99.9
3	Butanol	70.6	90.1
4	Pentanol	46.0	99.9
5	Hexanol	61.3	99.4
6	Octanol	46.0	91.8

[a] Reaction conditions: molar ratio of SA to alcohol, 1:3; temperature, 368 K; time, 12 h; catalyst weight, 0.4 g.

[b] Selectivity for esters (base on salicylic acid).

6. Recycling capability of $Ce(SO_4)_2$/001×7

The reusability of $Ce(SO_4)_2$/001×7 was examined using salicylic acid and methanol as model substrates. After reaction, $Ce(SO_4)_2$/001×7 was readily separated and washed with diethyl ether for three times. After removal of water at 80ºC for 6 h, it could be directly used for the next cycle. As is shown in Fig. 7, the conversion of SA decreased from 93.3% to 80.0% after reusing for 5 times. The decrease of the reusability may be attributed to the swelling effect of the resin and the loss of active sites after reaction[33]. Besides, the selectivity for methyl salicylate of all cases was more than 99.0%.

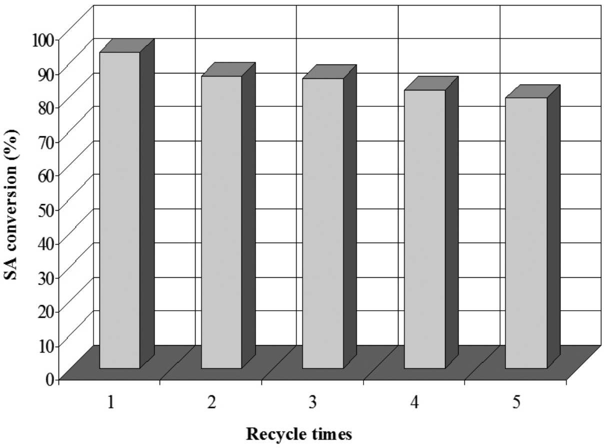
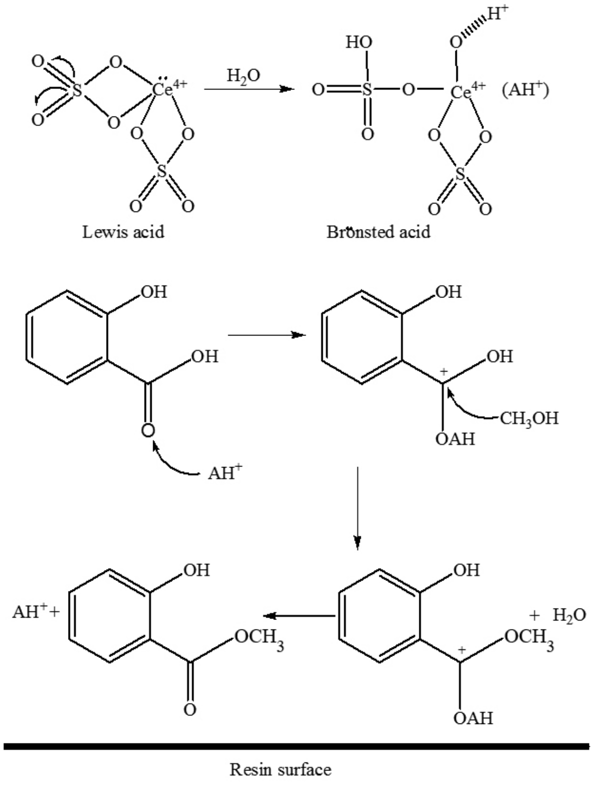


Figure 7 Esterification of salicylic acid with methanol, the reusability of catalyst $Ce(SO_4)_2$/001×7. Reaction conditions: molar ratio of SA to methanol, 1:3; temperature, 368 K; time, 12 h; catalyst weight, 0.4 g.

7. Mechanism of the esterification system

The esterification of salicylic acid with methanol is a nucleophilic substitution. This reaction was so slow that it needed to be activated by high temperature or a catalyst to facilitate the overall reaction[34, 35]. A possible mechanism of methyl salicylate formation was illustrated in Scheme 1, which involved the nucleophilic attack by methanol on carboxyl[27]. The observed activity could be explained as follows: On the surface of the resin, SA was absorbed and activated on the acid sites by its carbonyl oxygen, and then the formation of methanol attacking the unstabilizing cationic intermediate took place. After electron transfer reaction happened, the reaction product methyl salicylate could be obtained.



Scheme 1 Mechanism for methyl salicylate formation.

CONCLUSION

From the detailed studies on the esterification of salicylic acid with methanol, the following conclusion could be derived. A series of Ce^{4+} modified cation-exchange resins were successfully synthesized and showed high selectivity for methyl salicylate through the esterification of the –COOH group of salicylic acid while the –OH group remaining nearly unreacted. With the incorporation of $Ce(SO_4)_2$, the catalytic activity of the caion-exchange resins were greatly improved. Besides, the optimal reaction parameters for the synthesis of methyl salicylate were obtained. A mechanism that involved salicylic acid being activated on acid sites via its carbonyl oxygen and nuleophilic attack by methanol on the carboxyl atom was proposed.

ACKNOWLEDGMENTS

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