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Mild liquid-phase friedel-crafts acylation of thiophene to 2-acetylthiophene over solid-acid catalysts

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ABSTRACT

2-Acetylthiophene was synthesized by the acetylation of thiophene with acetic anhydride. Effects of solid-acid catalysts HZSM-5, NKC-9 and Hβ, reaction time and the molar ratio of acetic anhydride to thiophene were studied. Hβ showed excellent acetylation activity with almost 99% conversion of thiophene being obtained under conditions of normal pressure, reaction temperature 60°C and molar ratio of thiophene to acetic anhydride of 1:3. The yield of 2-acetyithiophene is 98.6%. The catalyst used can be recovered, regenerated and reused to give almost the same yield of 2-acetyithiophene as that given by the fresh Hβ zeolite.
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KEYWORDS

INTRODUCTION

2-acetylated thiophene, furan, pyrrole, pyridine are very important intermediates for the fine chemicals such as drugs and pharmaceuticals, flavouring agents for food stuffs[1, 2]. These compounds are generally produced by the conventional acetylation process, the famous Friedel–Crafts acetylation reaction, which is an electrophilic substitution reaction and takes place in the presence of Lewis acid–metal chlorides and some other solid catalysts, such as anhydrous $AlCl_3$[3-5]. However, the use of anhydrous $AlCl_3$ poses several problems, such as requirement of the reagent in stoichiometric quantities (particularly for the acylation reactions), difficulties in its separation from the reaction products, creation of a large volume of toxic liquid waste, very high moisture sensitivity that demands moisture-free substrate and reaction conditions, et al. Therefore, due to the technical and environmental problems, during the last decade great efforts have been performed to replace conventional homogeneous catalysts by recoverable and regenerable solid catalysts, such as heteropoly acids/salts, sulphated ZrO_2, Fe_2O_3 or Al_2O_3-ZrO_2[6-9]. However, those solid acid catalysts showed either lower activity in the acylation or high moisture sensitivity[10]. Zeolites, with their shape selective properties and good regenerability, have been found to be viable alternatives to liquid acids in numerous reactions in recent years. Acylation of aromatic compounds was reported using different kinds of zeolites[11-16].

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In this paper, HZSM-5 and Hβ zeolites were selected to be the solid-acid catalyst for Friedel–Crafts acylation of thiophene. A strong cation exchange resin, NKC-9 was used for comparison. The influences of the reaction temperature, the catalyst/substrate ratio and the molar ratio of thiophene to acetic anhydride have been explored. Additionally, the catalyst deactivation during the reaction, as well as its possibility for regeneration has been investigated.

EXPERIMENTS

Materials

Water glass liquid (SiO_2 26.5%, Na_2O 8.2%) was provided by Qingdao Dongyue sodium silicate Co., Ltd. $NaAlO_2$ (Al_2O_3 49%, Na_2O 38%) was provided by Zibo Li er chemical Co., Ltd. TEAOH (25%) and TPAOH (25%) were provided by Zhejiang Kente chemical co., Ltd. NaOH (96%), HCl (36%) and TEOS (28.4%) were provided by Sinopharm Chemical Reagent Co., Ltd. Thiophene (99.9%) and acetic anhydride (99.9%) were provided by Qingdao Hecheng pharmaceutical Co., Ltd.

Catalysts preparation

The Na-ZSM-5 (SiO_2/Al_2O_3=60) sample was made according to the method reported S. Wang, et al.[15] The H-Beta or HZSM-5 were obtained by ion-exchange method from Na-Beta (Provided by Shandong Qilu Huaxin High-tech. Co. Ltd., SiO_2/Al_2O_3=25, 30, 38 and 60) and NaZSM-5 as following[16]: Na-Beta was added into a 1.0 mol·L^{-1} of NH_4NO_3 aqueous solution and stirred at 80! for 3 h. The products were obtained by filtration, washed with distilled water and dried at 100! for 3 h. Finally, the products were calcined at 500! for 6h. NKC-9 was purchased from Nankai University Catalyst Co., Ltd., and used without any other treatment.

Catalyst characterization

X-ray diffraction (XRD) analysis was recorded on a DX2700 with Cu-Kα radiation, scanning from 5$^{æ\%}$ to 50$^{æ\%}$ (2θ) range. The voltage and current used were 40 kV and 30 mA at room temperature. The surface area of the catalyst was calculated by the BET/BJH method with N_2 adsorption and desorp-tion performed in a Micromeritics ASAP 2000 instrument. The NH_3-TPD measurements were carried out in Finesorb-3010 equipment with a thermal conductivity detector (TCD). Prior to the measurements, about 80 mg of the sample were flushed with helium (20 cm^3·min^{-1}) at 200!. After cooling at room temperature, ammonia adsorption was carried out during 30 min with an ammonia flow rate of 15 cm^3·min^{-1}. Physically adsorbed ammonia has been removed by purging with helium (20 cm^3·min^{-1}) for 30 min before the NH_3-TPD measurement. The NH_3-TPD of the samples was carried out by increasing the temperature linearly from 0! to 800! with a heating rate of 20 K·min^{-1}, and holding for 40 min following by a helium flow rate of 20 cm^3·min^{-1}, purging for 10 min under 800! and then cooled down to room temperature.

Acylation of thiophene and acetic anhydride

The acylation reactions were carried out in a 50 ml of round bottomed flask with a condenser, a thermometer and a magnetic stirrer under heating in water bath with acetic anhydride as acylating agent. A typical reaction was carried out as follows: 8.4 g (1.0 mol) of thiophene and 30.6 g (3.0 mol) of acetic anhydride were introduced in the flask. After that, 1.17 g of fresh catalyst were added to the reaction mixture and magnetically stirred. Small amount of samples were taken periodically at different time and analyzed by GC-14C (Shimazu, Japan) equipped with an FFAP capillary column and an FID detector.

RESULTS AND DISCUSSIONS

Effect of acid strength and acid amount

It has been investigated that Friedel–Crafts acetylation reaction is an electrophilic substitution reaction and takes place in the presence of Lewis acid catalysts. Therefore, we select three different solid acid (NKC-9, HZSM-5 and Hβ zeolites) as catalysts to investigate the catalytic conversion of thiophene into 2-acetylthiophene using acetic anhydride as acetylating agents. The results are displayed in TABLE 1.

It demonstrated that the strong acidic ion exchange resin (NKC-9) achieved significant activity for

	Conversion of thiophene at 3.0h / %	Selectivity /%	Yield / %
HZSM-5	18.2	99.1	22.3
Hβ	98.7	99.9	98.6
NKC-9	96.6	97.3	95.8

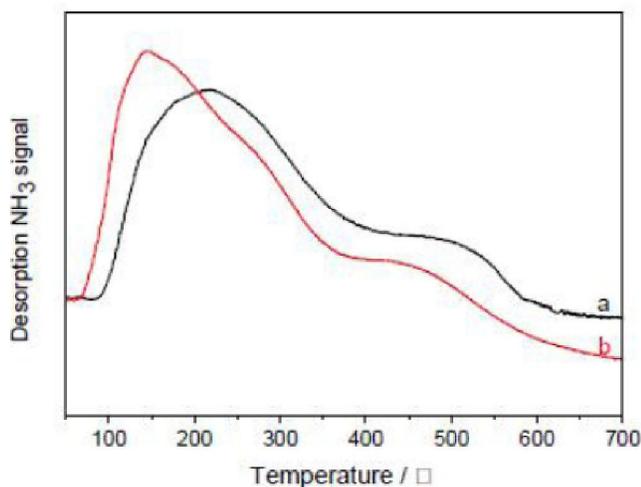Reaction condition: reaction temperature 333 K and molar ratio of thiophene to acetic anhydride $=1:3$.

TABLE 2 : Different crystalline sizes of HZSM-5, Hβ and NKC-9

Catalyst	Pore / nm	acid amount (mmol·g^{-1})
HZSM-5	0.56	1
Hβ	0.77	0.45
NKC-9	58	4.6

Note: The acid quantity of strongly acidic ion exchange resin (NKC-9) was measured by potentiometric titration method

thiophene conversion. However, the zeolite catalysts, HZSM-5 and Hβ with the ordered structure, showed good selectivity to 2-acetylthiophene. Hβ zeolite catalysts showed higher activity in the acetylation reaction due to their higher pore size than HZSM-5. Unfortunately, the conversion of thiophene is very poor over HZSM-5 and the selectivity to 2-acetylated thiophene over NKC-9 is not good.

The NH$_3$-TPD patterns of the samples are shown in Figure 1. As shown, the two peaks of NH$_3$ desorption ascribed to desorption of ammonia from the weaker acidic sites and stronger acidic sites, respectively. The number of weak acidic sites is much greater than the number of strong acidic sites. Moreover, HZSM-5 shows a lot stronger acidic sites than Hβ zeolite.

The results of conversion of thiophene and selectivity to 2-acetylthiophene demonstrated that the structure, acidity and surface property of the solid acid catalysts determine the acetylation of thiophene. The NKC-9 is a kind of strong acidic ion exchange resin, it shows only strong acidity.

TABLE 2 shows that the average pore diameters of Hβ and NKC-9 were larger than HZSM-5, the largest average pore diameter is beneficial for this reaction. For the HZSM-5 zeolite, the activity is probably limited by steric and diffusional hindrances, as a consequence of its small micropore size compared to that of the molecules involved in the reaction[17].

Effect of the reaction temperature

The influence of the reaction temperature on the conversion of acetylation of thiophene with acetic anhydride was evaluated at three different temperatures (313K, 333K and 353K) over the Hβ catalyst with a molar ratio of thiophene to acetic anhydride of 1:3, and a percentage of catalyst to substrate of 3%. Figure 2 shows the effect of reaction temperature on the progress of total conversion with time.

Figure 1 : NH$_3$-TPD patterns of samples: (a) HZSM-5, (b) Hβ
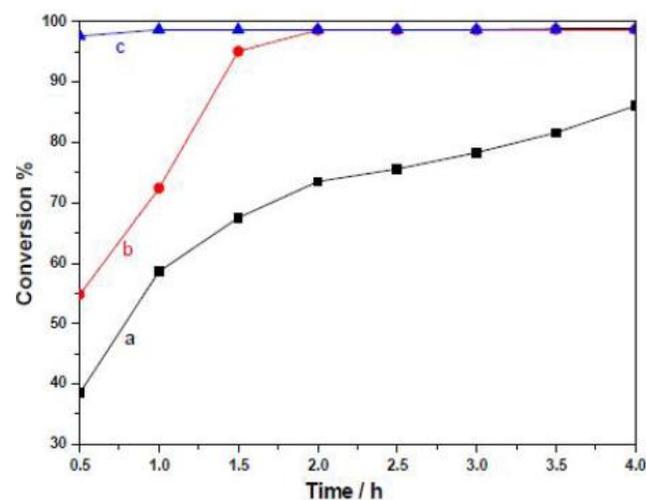
Figure 2 : The conversion of thiophene over Hβ at (a) 313K (b) 333K and (c) 353K

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It can be found that higher reaction temperature can improve the efficiency of acetylation, which in turn enhances the mean yield. When the reaction was carried out at 313 K, the conversion of thiophene is very low, and for about 0.5h of reaction, less than 40% of thiophene was converted to products. 4 hours' reaction cannot lead to the total conversion of thiophene. When the reaction temperature was improved to 333K, the total conversion of thiophene can be found at 2 h, while at 353 K, total conversion of thiophene needs 30 min.

The acetyl group can be introduced into either 2-site or 3-site on the thiophene ring. As the pharmaceutical intermediates, the substitution of 3-sites to form 3-acetyl heterocyclic compounds is disadvantage to the quality of the end products, and the removal of the byproduct requires special and tedious efforts in the additional step. Therefore, avoiding the generation of byproduct 3-acetyl heterocycle is an essential operation. It can be found that a high selectivity for 2-acetylthiophene is obtained at lower temperatures due to the poor diffusion of the primary products of thiophene. However, the selectivity for 2-acetylthiophene decreases obviously with arise in temperature from 313K to 353K. At high temperature, the rapid diffusion of thiophene can suppress the subsequent acetylation reactions effectively, which may lead to a significant decrease in the selectivity for 2-acetylthiophene and improve in

the selectivity for by-product 3-acetyithiophene[18].

Higher reaction temperature can improve the efficiency of acetylation reaction, which in turn enhances the mean yield. On the contrary, the mean yield decreases significantly when the reaction temperature is higher than 353 K. One reason may be offered to explain why the reaction temperature at 353 K resulted in a lower mean yield than at 333 K. The boiling temperature of thiophene is about 357 K. The thiophene started volatilization when the reaction temperature exceeded 353 K. The volatilization of thiophene might reduce the yield. In short, the optimal level of reaction temperature might be 353K.

Effect of feed ratio

Figure 3 shows the yields of 2-acetylthiophene versus time in the acetylation of thiophene with acetic anhydride over Hβ at different thiophene/acetic anhydride ratios. It demonstrated that the mean yield increased when the thiophene/acetic anhydride molar ratio increased from 1:2 to 1:4. Increasing thiophene/acetic anhydride molar ratio can improve the efficiency of acetylation, which in turn enhances the yield.

With a 1:4 thiophene to acetic anhydride ratio the reaction was slightly faster than 1:2 and 1:3 at 1.5h, an increase in the reaction time causes a significant enhancement of the thiophene conversion into
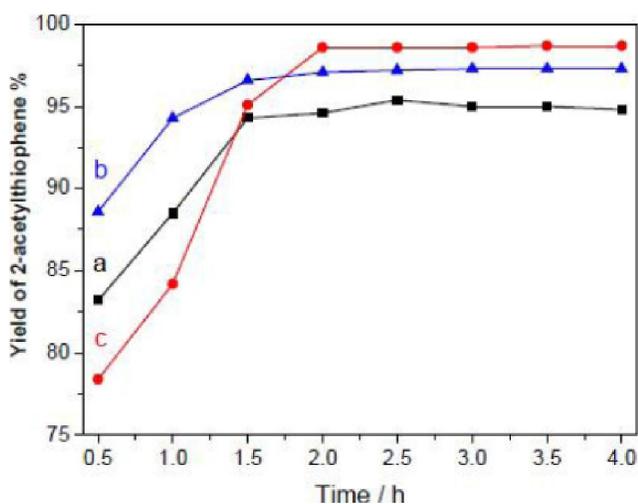

Figure 3 : Conversion versus time curves in the acylation of thiophene with acetic anhydride over Hβ at different thiophnen/acetic anhydride ratios of (a) 1:2; (b) 1:3 (c) 1:4. (Reaction conditions: 333 K, 3wt.% catalyst)

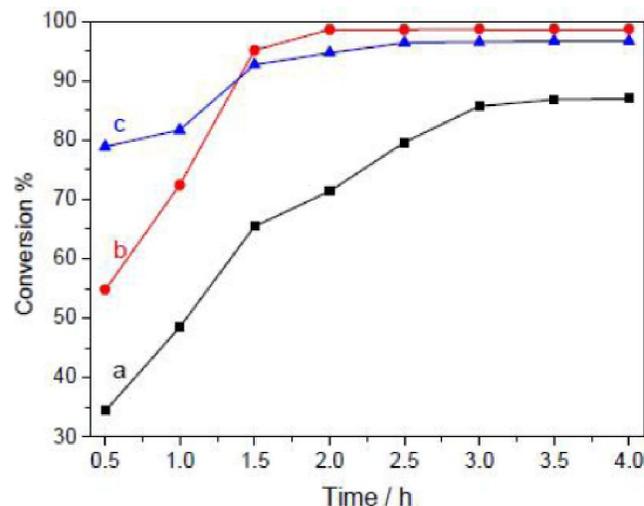**Figure 4 : Conversion of thiophene versus time in the acetylation of thiophene with acetic anhydride over Hβ with a percentage of (a) 2%, (b) 3%, (c) 4%**

2-acetylthiophene at 1:3, At lower ratios of 1:2, acylation was, as expected, slower due to the deactivation of the catalyst probably resulting from the competitive adsorption of the reactants[19]. At higher ratios (1:4), not only the contact area of the thiophene and acetic anhydride decrease, but also it introduces a lot of trouble by the next-processing of the reaction. In short, there is an optimal level of thiophene/acetic anhydride molar ratio which might be 1:3.

Effect of the catalyst amount

The effect of the amount of catalyst used in the reaction has been investigated by varying the amount of catalyst introduced in the reactor. The others operation variables are kept constant. As illustrated in Figure 4, the thiophene conversion increases with the catalyst amount for all the reaction times, which means that not only the reaction rate at short times but also the maximum conversion obtained in the plateau at long times are enhanced by the catalyst concentration. The acetylating reaction is an exothermic reaction, the temperature is not easy to be controlled. If plenty of catalyst was used, the reaction temperature will be much high, and thus lead to the production of a lot of by-product 3-acetyithiophene, which is disadvantage to the quality of the end products.

Regeneration of the zeolites

Reusability of Hβ zeolites was investigated and the results are given in Figure 5. The regenerated
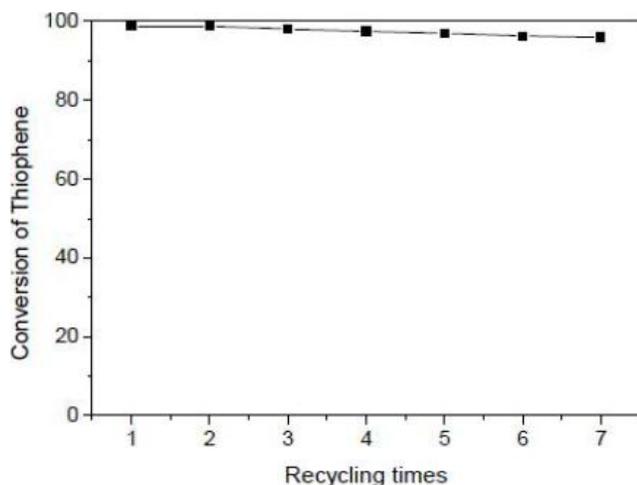
Figure 5 : Conversion of thiophene versus recycling times in the acetylation of thiophene with acetic anhydride over Hβ

zeolites almost displayed the same trend profiles with the reactive time and performances as their origins. Figure 5 also shows that the zeolites Hβ could be regenerated and recycled through calcination at high temperature. It indicates that the activity and stability of the zeolite can be regenerated efficiently and satisfactorily, which means that most of the acid sites can be regenerated to its original states. Therefore, the zeolites Hβ are expected to replace the traditional Lewis acid and Bronsted acid catalysts to solve the manufacturing and environmental problems.

CONCLUSIONS

This study reveals that the 2-acetylthiophene can be synthesized by acetylation of thiophene with acetic anhydride over solid-acid catalysts Hβ. Hβ showed excellent acetylation activity with all most 99ÿconversion of thiophene being obtained under conditions of normal pressure, reaction temperature and molar ratio of thiophene to acetic anhydride of 1:3, the yield of 2-acetyithiophene is 99.6%.

ACKNOWLEDGEMENTS

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