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Research Article

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Synthesis of ethyl vanillin using continuous flow microfluid technique

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ABSTRACT

We employed microfluid technique to synthesize ethyl vanillin by using microfluid technique. The structure of obtained ethyl vanillin was characterized by FTIR. The conditions of reaction temperature, flow velocity and the amount of raw materials were investigated and optimized to produce ethyl vanillin with high yield. The optimized experimental results indicated that using o-ethoxyphenol and chloroform as the main raw materials in the presence of phase-transfer catalyst of triethylamine will induce the Reimer-Tiemann reaction to form ethyl vanillin. The molar ratio was o-ethoxyphenol: chloroform: sodium hydroxide: triethylamine = 1:1.2:4.0:0.025, reaction temperature was 55 ℃ and flow rate was 6 mL/min. Results revealed that this method had features of short technological process and convenient manipulation. Under the optimal conditions, the yield ratio of ethyl vanillin was up to 82.3%.

Key words: Micro-fluid; Continuous flow preparing method; Ethyl vanillin

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INTRODUCTION

Microfluid concerns small (from 10^{-9} to 10^{-18} liter) volumes of fluids, using channels with dimensions from tens to hundreds of micrometers [1,2]. Microfluid is an intrinsically interdisciplinary field of science that embraces research in physics, chemistry, engineering, materials science, and biology [3-6]. The past decade witnessed rapid advancement in the area of chemical and materials synthesis. Microfluid technique, which as a novel method for the preparation of organic compounds, has attracted much attention in recent years [7-10]. Compared with the traditional tubular reactor, continuous flow microfluid technique (MF) has some advantages such as fewer reagent consumption, reaction temperature and time can be precisely controlled, high mass transfer rate, safety and easy manipulation[11-14]. Therefore, it exhibits unique superiority in the field of organic synthesis.

Ethyl vanillin is an important synthetic perfume, which can be widely used in food and cosmetics [15-17]. The methods for preparing ethyl vanillin usually involve safrole, P-hydroxy benzaldehyde, catechol, protocatechuic aldehyde, p-cresol and pyrocatecholmonoethyl ether. However, these methods have some drawbacks such as requiring long reaction time and harsh conditions. So the key point of developing new approach to synthesize ethyl vanillin is introducing aldehyde groups in the para-position of o-ethoxyphenol.

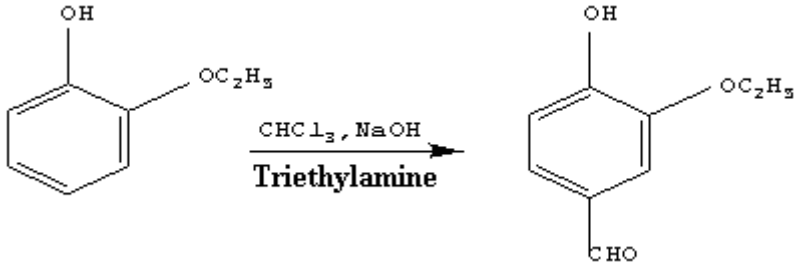
This work employed continuous flow micro-fluid technique to obtain ethyl vanillin with high yield. The advantage of this method was making the reaction temperature, time and the amount of raw materials controllable, which will facilitate the reaction procedure.

EXPERIMENTAL SECTION

2.1 Methods

Taking o-ethoxyphenol and chloroform as the main raw materials, with adding a certain amount of 95% ethanol,

sodium hydroxide and triethylamine, the product will be obtained via Reimer-Tiemann reactions. The equation is as follows:



2.2 Reagents and instruments

O-ethoxyphenol, AR (⩾90%) was purchased from Taixing Zhongran Chemical CO., LTD.; Triethylamine, AR(⩾ 96%), ethanol, sodium hydroxide (NaOH) and Diethyl ether were provided by Shanghai Zhongshi Chemical CO., LTD.; Chloroform and sulphuric acid were purchased from Shanghai Shenxiang Chemical CO., LTD.

The micro-fluid device (CMPR-T1) was purchased from Dalian Micro Chem CO. LTD(China); The micro mixer(SIMM-V2-Lasab45200) was purchased from Institute of Microtechnic Mainz GmbH(Germany); FT-IR Spectrometer(NEXUS-670) was purchased from Nicolet Instrument Corrp.

2.3 Experimental methods

2.3.1 Preparation of solution

0.05 mol of o-ethoxyphenol, 20 mL of ethanol, a certain amount of NaOH and triethylamine were added into a conical flask under stirring; another conical flask was added with chloroform to some amount.

2.3.2 Preparation procedure

Two streams were mixed in a micro-reactor with cross finger type. The reaction was carried out in the electric delay fuse by controlling the temperature needed. The device was installed with temperature sensor in the exit of mixing unit, which was used to detect the stream temperature. Moreover, double-pipe heat exchanger was installed. The experimental process was illustrated in Figure 1.

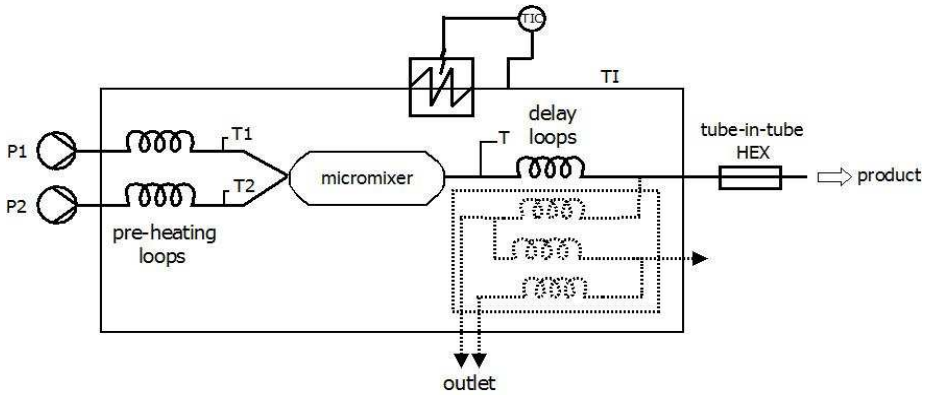


Fig.1 Schematic diagram of micro-fluid synthesis apparatus

2.3.3 Separation and purification of the product

Sulfuric acid was added to the cooling product until pH 2-3. At this moment, the solution was changed to dull-red and some crystalline solids are formed. The obtained product was washed and filtered with ethanol for three times. The filtrate was distilled under the water vapor until no oil droplets could be observed. The residual was cooled to form red solids and extracted with diethyl ether for three times. At last, the diethyl ether was distilled and red solids were obtained. The prepared solids were dissolved in hot water to separate impurities, after cooling, filtering and drying; the yellow crystalline ethyl vanillin was formed.

RESULTS AND DISCUSSION

3.1 FTIR

Figure 2 was FTIR pattern of ethyl vanillin. The peaks located at 3364cm-1 and 1043cm-1 were respectively corresponded to the stretching vibration of O-H in the benzene ring and C-O between hydroxyl and benzene ring. Peaks of 1675cm-1, 1605cm-1, 1579cm-1, 1515cm-1 were indexed with skeletal vibration of C=C in the benzene ring. Peaks of 1255cm-1 and 1043cm-1 were caused by the stretching vibration of Ar-O between ethyoxyl and

benzene ring and R-O(R=C2H5) in the ethyoxyl. Peaks of 2829cm-1 and 2723m-1 were corresponded to the stretching vibration of –CHO. Peaks of 754cm-1, 782cm-1,816cm-1 were typical absorptions of ortho-, meta-, and para-substitution, respectively. It was confirmed that the obtained material was ethyl vanillin.

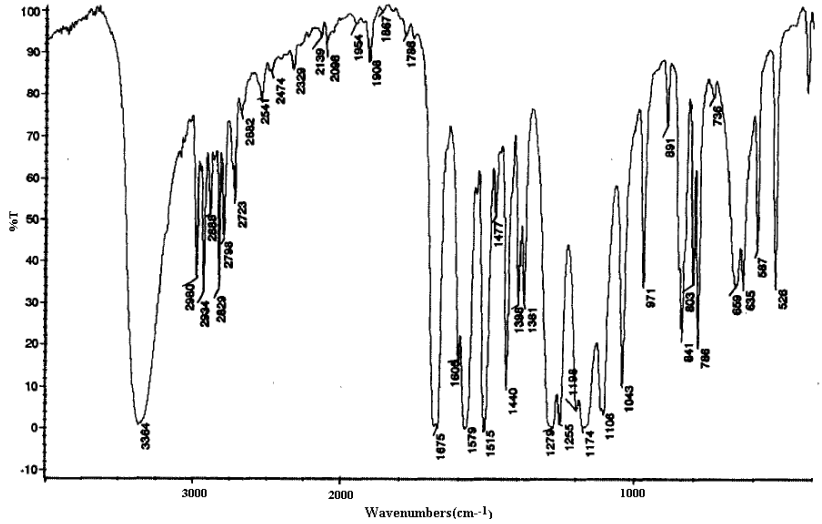


Fig.2 FTIR spectrum of ethylvanillin

3.2 Optimized synthesis conditions of ethyl vanillin

The yield rate of ethyl vanillin was set as the target, we investigated the reaction temperature, flow rate and the amount of raw materials to determine the best reaction conditions.

3.2.1 The effect of NaOH usage on the yield

Reaction conditions: The amount of ethoxyphenol, ethanol and chloroform was 0.05 mol, 20 mL and 0.08mol, respectively. The ratio of triethylamine to ethoxyphenol was 2.5%, The reaction temperature, flow rate and the volume of electric delay fuse was 55℃, 6mL/min and 45 mL, respectively.

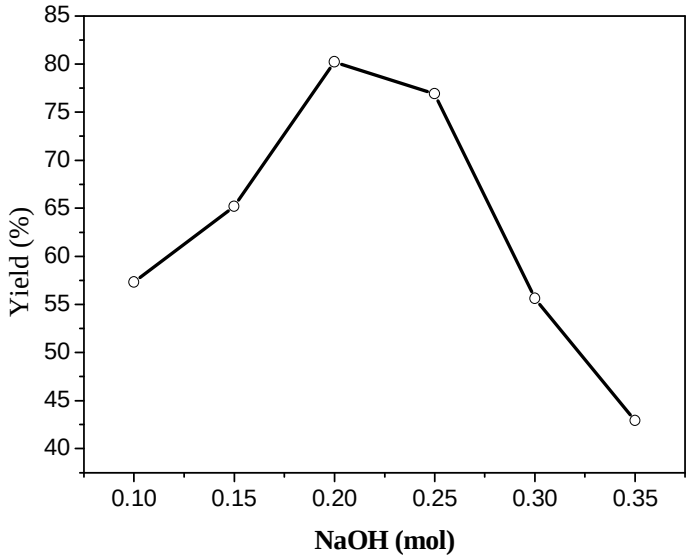


Fig.3 The effect of NaOH usage on the yield

The results were shown in Figure 3. When the amount of NaOH was between 0.15mol and 0.25mol, the product yield was ascend linearly. When the amount of NaOH was higher than 0.25mol, the yield rate decreased significantly. The reason was that NaOH played an important role in adjusting the pH values. However, NaOH would react with chloroform when the usage was higher than a critical value, which would induce the low yield. The best amount of NaOH in this experiment was 0.2mol.

3.2.2 The effect of chloroform usage on the yield

Reaction conditions: The amount of ethoxyphenol, ethanol and NaOHwas 0.05 mol, 20mL and 0.2 mol, respectively. The ratio of triethylamine to ethoxyphenol was 2.5%, the reaction temperature, flow rate and the volume of electric delay fuse was 55℃, 6mL/min and 45 mL, respectively.

The results were shown in Figure 4. When the amount of chloroform was between 0.02 and 0.08mol, the product yield was ascend linearly. When the amount of chloroform was between 0.06 and 0.08mol, the highest yield was produced. When the amount of chloroform was higher than 0.08mol, the yield was decreased. The reason was that chloroform would be polymerized when the usage was higher than a critical value. The best amount of chloroform in this experiment was 0.08mol.

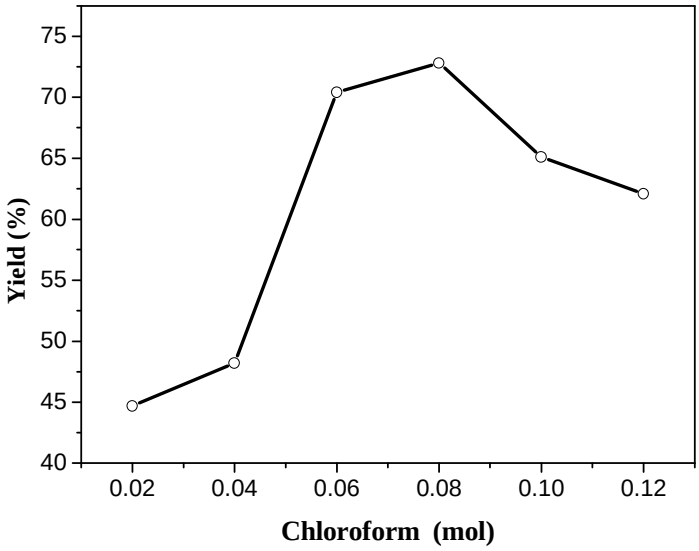


Fig.4The effect of chloroform usage on the yield

3.2.3 The effect of triethylamine usage on the yield

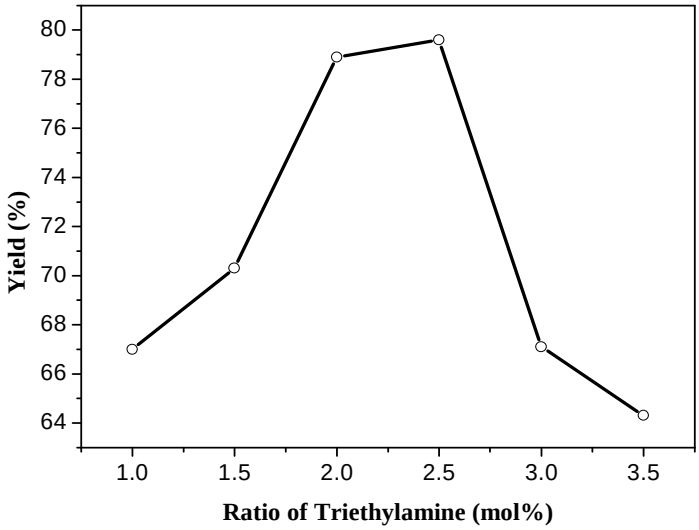


Fig.5 The effect of triethylamine usage on the yield

Under the optimized conditions, the effect of triethylamine usage on the yield was proposed, the results were shown in Figure 5. When the ratio of triethylamine to ethoxyphenol was 2.0~2.5%, the highest yield would be obtained. When the ratio was 1-1.5% and 3%, the yield rate was very low. Therefore, the determined ratio of triethylamine to ethoxyphenol was 2.5%.

3.2.4 The effect of reaction temperature on the yield

Reaction conditions: The amount of ethoxyphenol, ethanol, chloroform and NaOH was 0.05 mol, 20mL, 0.06mol and 0.2 mol, respectively. The ratio of triethylamine to ethoxyphenol was 2.5%, the flow rate was 6mL/min and the volume of electric delay fuse was 45 mL.

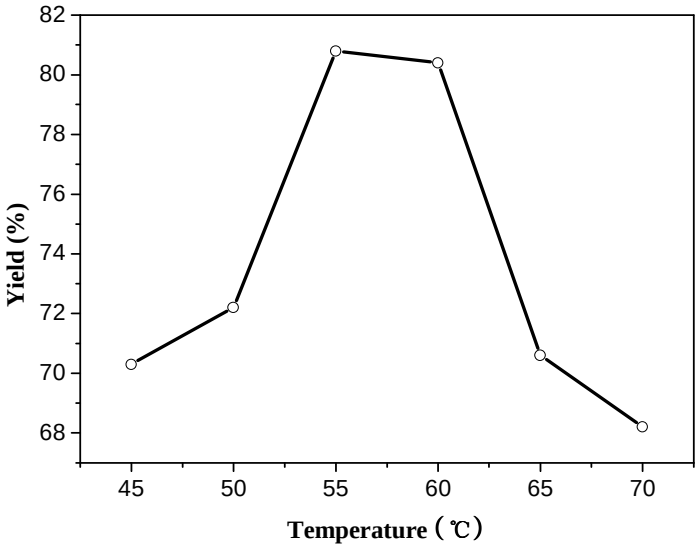


Fig.6 The effect of reaction temperature on the yield

The results were shown in Figure 6. When the reaction temperature was 55~60℃, the yield was as high as 81%. The yield decreased when the temperature lower than 55℃ or higher than 60℃. The accounts for the reason were that the number of active molecule was relatively fewer when the temperature was low. This would result in the incomplete reaction and induce the low yield. On the contrary, when the temperature over 60℃, the positive reaction would be enhance, which was favorable for the formation of byproduct pix. The determined temperature was 55℃。

3.2.5 The effect of flow rate on the yield

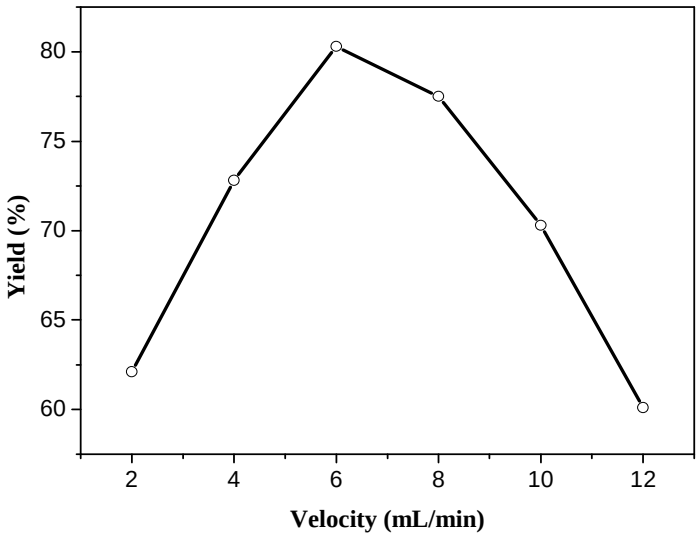


Fig.7The effect of flow rate on the yield

Under the optimized conditions, the effect of flow rate on the yield was shown in Figure 7. When the flow rate was 2-8 mL/min, the product yield was ascend linearly. However, the yield rate decreased when the flow rate over 8mL/min. So the flow rate was set as 6 mL/min.

CONCLUSION

Taking o-ethoxyphenol and chloroform as raw materials in the presence of phase-transfer catalyst of triethylamine will induce the Reimer-Tiemann reaction to form ethyl vanillin. The molar ratio was o-ethoxyphenol: chloroform: sodium hydroxide: triethylamine = 1:1.2:4.0:0.025, reaction temperature was 55℃ and flow rate was 6 mL/min. Under the conditions, the yield rate of ethyl vanillin was 82.3%. This method had features of short technological process and convenient manipulation.

Acknowledgements
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