Study on optimum synthesis of ethyl cyanoacetate

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Abstract. Ethyl cyanoacetate is an important chemical intermediate and has been used widely. Ethyl cyanoacetate was prepared by esterification of cyanoacetic acid and absolute ethanol with mixed catalyst (the same proportion of silicotungstic and p-toluene sulfonic acid as catalyst). The influence factors of the amount of catalyst, n(cyanoacetic acid): n (absolute ethanol), reaction time and reaction temperature on the esterification rate was investigated by orthogonal experiment of four factors and three levels. The product was analyzed by gas chromatography to determine the optimum reaction conditions.

1 Introduction
Ethyl cyanoacetate molecular formula is C₇H₉NO₂ and structural formula is NCCH₂COOCH₃H₃. Ethyl cyanoacetate is an intermediate of fine chemical products such as medicine and dyes [1]. It is also used in the synthesis of esters, amides, acids and nitriles [2]. It is an intermediate for the preparation of 2-amino-4, 6-dimethoxypyrimidine, which can be prepared as an intermediate for sulfonyleurea herbicides, as well as an intermediate for the insecticide flufenitri [3]. There is a wide range application prospects for ethyl cyanoacetate [4].

At present, the main methods for preparing ethyl cyanoacetate are as follows: Ethyl chloroacetate cyanidation method, methyl cyanoacetate transesterification method, cyanoacetate esterification method etc. are used frequently. Catalysts are important in the synthesis of ethyl cyanoacetate, such as heteropoly acid. Heteropoly acid, as a catalyst with less environmental pollution, there is strong acidity and oxidation reducibility, and the advantages of stable structure, high activity, non-corrosive equipment, little pollution, etc. [5]. Heteropoly acid is a good catalyst in esterification reaction.

Silicotungstic acid was used in this experiment. Ethyl cyanoacetate was prepared by esterification of cyanoacetic acid and absolute ethanol. The factors influencing the esterification rate, such as catalyst dosage, reaction time, reaction temperature, were analyzed. Optimization conditions were obtained through orthogonal experiment.

2 The experiments

2.1 Materials
Cyanoacetic acid (Yingkou sanzheng Fine Chemical Co., LTD.), absolute ethanol, silicotungstic acid, p-toluene sulfonic acid (Tianjin Zhiyuan Chemical Reagent Co., LTD.), phosphomolybdic acid, phosphotungstic acid (Sinopac Chemical Reagent Co., LTD.), 99% ethyl cyanoacetate, benzene (Alighting Reagent Co., LTD.).

2.2 Apparatus
Main experimental instruments required for the experiment :JJ-1 Precision electric mixer (Zhengzhou Ganzheng Equipment Co., LTD.), SP2100A gas chromatograph (Beijing Beifen-Ruili Analytical Instrument Group Co., Ltd.), etc.

2.3 Experiment methods
The device used in this experiment is shown in Figure 1.

Fig. 1 Reaction device diagram
1-electric agitator 2-thermometer 3-water konckout vessel 4-four-necked flask 5-heating device

In this experiment, ethyl cyanoacetate was prepared by esterification of cyanoacetic acid and absolute ethanol. Cyanoacetic acid, absolute ethanol and catalyst were added into four-necked flask and stirred with an electric agitator to make the evaporated water and absolute ethanol flow back to the water separator through the condensing pipe. Gas chromatography analyzer was used for analysis and internal standard method was used for calculation.
3 Results and discussion
The catalyst was examined firstly, then the single factor experiments and orthogonal experiment were carried out, and the results were analyzed to determine the optimum reaction conditions.

In this experiment, benzene was used as the internal standard, 99% pure ethyl cyanoacetate was used as the reference substance. The correction factor was calculated, and then the correction factor was used to calculate the content of ethyl cyanoacetate prepared.

Gas chromatography conditions: The column is KB-1, the carrier gas is nitrogen, the detector is FID, and the temperature is programmed. The inlet temperature is 240℃, the initial temperature of the column box is 120℃, and the heating rate is increased at 30℃/min. The temperature was maintained at 205℃ for 5 minutes and the detector temperature was 255℃.

The calculation formula of correction factor 1 is as follows:

\[ f = \frac{m_i/m_r}{A_i/A_r} \times \frac{A_i}{m_i} \times \frac{A_r}{A_i} = \frac{m_i}{m_r} \times \frac{A_i}{A_r} \]  

\[ f = 2 \times \frac{56.2}{39.4} = 2.85 \]  

The chromatogram of the first correction factor is shown in Figure 2, and table(1) is description of gas chromatogram.

Fig. 2 chromatogram
Table(1 ) Gas chromatogram description

| NO. | Retention time | Peak area % | Peak area |
|-----|----------------|-------------|-----------|
| 1   | 0.502          | 4.373       | 39008     |
| 2   | 0.573          | 56.23       | 501528    |
| 3   | 0.800          | 39.4        | 351413    |
| total | 100             | 891949      |           |

The second correction factor is calculated:

\[ f = \frac{m_i/m_r}{A_i/A_r} \times \frac{A_i}{m_i} \times \frac{A_r}{A_i} = \frac{2}{1} \times \frac{57.9}{38.9} = 2.97 \]  

In both experiments, there will be a peak diagram of ethanol, and the absolute ethanol should be residual, but there is no influence on the experimental results and will not affect the results of the correction factor.

According to the above data, results of data are shown in Table1.

Table1 Correction factor data

| No. | Correction factor | Average value |
|-----|-------------------|--------------|
| 1   | 2.85              |              |
| 2   | 2.97              | 2.90         |
| 3   | 2.89              |              |

From the above algorithm, it can be seen that the correction factor is obtained when the quality ratio is 1:1, results are shown in Table 2.

Table 2 Correction factor data

| No. | Correction factor | Average value |
|-----|-------------------|--------------|
| 1   | 2.94              |              |
| 2   | 2.83              | 2.88         |
| 3   | 2.87              |              |

3.2 Calculation of esterification rate

Fig.3 is a gas chromatogram using mixed catalyst. Taking Fig.3 as an example and table(2) is description of gas chromatogram.
### 3.3 Analysis of esterification results

Single-factor experiment was carried out to investigate the type of catalyst, dosage of catalyst, reaction time, molar ratio of cyanoacetic acid to absolute ethanol, and reaction temperature respectively.

#### 3.3.1 Orthogonal experimental results

According to the single factor experiment, the orthogonal experiment with four factors and three levels was used to determine the optimum reaction conditions. The table of factor levels is shown in Table 4, and the experimental result is shown in Table 5.

![Fig. 4 Chromatogram of optimum reaction conditions](image_url)
Table(3) Gas chromatogram description

| NO. | Retention time | Peak area % | Peak area |
|-----|----------------|-------------|-----------|
| 1   | 0.165          | 0.007241    | 71        |
| 2   | 0.284          | 0.004478    | 44        |
| 3   | 0.375          | 0.1555      | 1523      |
| 4   | 0.448          | 0.1473      | 1444      |
| 5   | 0.503          | 23.35       | 228749    |
| 6   | 0.574          | 50.79       | 497620    |
| 7   | 0.728          | 0.0475      | 465       |
| 8   | 0.802          | 23.96       | 234735    |

| total | 100 | 964651 |

4 Conclusions

The catalyst used in the esterification of cyanoacetic acid and absolute ethanol was determined to be the same proportion of silicotungstic acid and p-toluene sulfonic acid.

It is found that the most important factor affecting the esterification rate of ethyl cyanoacetate is the amount of catalyst, followed by the molar ratio, esterification temperature and esterification time by analysis of orthogonal experiments, and the optimum reaction conditions are determined by orthogonal experiments as follows: The molar ratio of cyanoacetic acid and absolute ethanol was 1.3.5, the reaction time was 3.5h, the reaction temperature was 80 ℃ and the amount of catalyst was 1.5%.

The esterification rate of optimum conditions was analyzed by gas chromatograph and calculated by internal standard method. The esterification rate was 91.5%.

Acknowledgments

Thanks to the guidance program of Liaoning Key Laboratory of Chemical Additive Synthesis and Separation.

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