EFFECTS OF THE DIFFERENT REACTION CONDITIONS ON SYNTHESIZING OF ISOPROPYL CHLOROACETATE

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In the present article the effects of different reaction conditions on the synthetic method of isopropyl chloroacetate have been reviewed. Different catalysts that consist of inorganic salt like ($Ce(SO_4)_2{\cdot}4H_2O$ and $NaHSO_4$) and PCl_3 have also been introduced. The reaction conditions include the reaction time, the molar ratio of chloroacetic acid to isopropanol, the amount of the catalyst and the number of reusable catalyst. The optimized reaction time, the molar ratio of chloroacetic acid to isopropanol and the amount of the catalyst are beneficial to improve the yield of isopropyl chloroacetate.

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INTRODUCTION

Isopropyl chloroacetate is one of the important organic chemical materials and intermediates. Isopropyl chloroacetate is used as an organic solvent and as an intermediate for synthesis of pharmaceuticals, mainly non-steroid anti-inflammatory drugs such as naproxen and ketoprofen[2]. Its molecular formula, boiling point, relative density (25 °C), refractive index n_D^{20} and flash point are $C_5H_9O_2Cl$, 149.5 °C, 1.0812, 1.0423 and 56 °C.[1] Requirements for isopropyl chloroacetate are gradually increased in *China*. The main manufacturing process has two types of methods. The first method is that chloroacetic acid and isopropanol as feedstocks and BF_3 as a catalyst are used to produce isopropyl chloroacetate. In the other method the catalyst is concentrated sulphuric acid. These methods have a lot of disadvantages, such as more secondary reaction taking place, low yield and purity of isopropyl chloroacetate. [3]

In the present paper, different catalysts such as inorganic salt ($Ce(SO_4)_2{\cdot}4H_2O$ and $NaHSO_4$) and PCl_3 have been evaluated in the synthesis of isopropyl chloroacetate. Effects of different reaction conditions, such as the reaction time, the molar ratio of chloroacetic acid to isopropanol, the amount of the catalyst and the number of reusable catalyst, on the synthetic method of isopropyl chloroacetate have been reviewed. Furthermore, the optimized reaction conditions are also pointed out.

DISCUSSION

Effects of the reaction time on the yields of isopropyl chloroacetate by the addition of $Ce(SO_4)_2{\cdot}4H_2O$ as a catalyst

Yang Liangzhun [4] developed a method for the preparation of isopropyl chloroacetate and effects of the reaction conditions on its yield were discussed. Using $Ce(SO_4)_2{\cdot}4H_2O$ as a catalyst and chloroacetic acid and isopropanol as feedstocks, isopropyl chloroacetate was generated. It was observed that the molar ratio of chloroacetic acid to isopropanol and the amount of $Ce(SO_4)_2{\cdot}4H_2O$ were kept constants and were 1.0:1.3 and 3.5 % of chloroacetic acid weight, respectively. Effects of the reaction time on the yields of isopropyl chloroacetate had also been discussed. Table 1 showed the effect of reaction time on the yield of isopropyl chloroacetate. The experimental results showed that the yield of isopropyl chloroacetate increased with an increase of the reaction time. When the reaction time was 4 h, the maximum yield of isopropyl chloroacetate was 98.62%, so the optimized reaction time was proved to be 4 h.

Table 1. Effect of the reaction time on the yield of isopropyl chloroacetate

Reaction time, h	1.0	2.0	2.5	3.0	4.0
Yield, %	57.42	79.12	84.29	97.50	98.62

The effect of the molar ratio of chloroacetic acid to isopropanol on the yield of isopropyl chloroacetate by the addition of $NaHSO_4$ as a catalyst

Zhang Jie [5] explained why $NaHSO_4$ as a catalyst could occupy the concentrated sulfuric acid to generate isopropyl chloroacetate. The reaction time and the amount of $NaHSO_4$ were kept at constants at 3.0 h and 1.0 % of chloroacetic acid weight, respectively. Effects of the molar ratio of chloroacetic acid to isopropanol on the yield of isopropyl chloroacetate had been discussed. Table 2 showed the effect of molar ratio of chloroacetic acid to isopropanol on the yield of isopropyl chloroacetate. The yield of isopropyl chloroacetate firstly increased and then decreased with an increase in the molar ratio of chloroacetic acid to isopropanol. When the molar ratio of chloroacetic acid to isopropanol was 1.0:1.2, the maximum yield of isopropyl chloroacetate reached the value of 82.4%. $NaHSO_4$ can be used to produce isopropyl chloroacetate because it was very cheap, stable and insoluble in organic acids and organic alcohol. After the reaction was done, $NaHSO_4$ as insoluble material can easily be separated from the reaction system.

Table 2. Effect of the molar ratio of chloroacetic acid to isopropanol on the yields of isopropyl chloroacetate

Molar ratio	1.0:1.0	1.0:1.1	1.0:1.2	1.0:1.3	1.0:1.4
Yield, %	60.6	72.7	82.4	77.3	72.1

Effects of the amount of PCl_3 on the yields of isopropyl chloroacetate by the addition of PCl_3 as a catalyst

Liang Chugen[6] described the principles of isopropyl chloroacetate synthesis and discussed the effect of reaction conditions on the yield of isopropyl chloroacetate. The reaction time and the molar ratio of chloroacetic acid to isopropanol were kept to be constant at 2.0 h and 1.0:1.4, respectively. Effects of the amount of PCl_3 on the yield of isopropyl chloroacetate had been discussed. The effect of the amount of PCl_3 on the yields of isopropyl chloroacetate is presented in Table 3. The yield of isopropyl chloroacetate firstly increased and then decreased with an increase in the amount of PCl_3. When the amount of PCl_3 was 6.7 % of chloroacetic acid weight, the maximum yield of isopropyl chloroacetate reached the value of 89.5%.

Table 3. The effect of PCl_3 amount on the yields of isopropyl chloroacetate

Amount of PCl_3, ml	0.5	1.0	2.0
Yield, %	71.0	89.5	82.0

Effects of the number of reusable $Ce(SO_4)_2{\cdot}4H_2O$ on the yields of isopropyl chloroacetate by the addition of $Ce(SO_4)_2{\cdot}4H_2O$ as a catalyst

Yang Liangzhun [4] introduced a synthetic method of isopropyl chloroacetate and evaluated the effect of reaction conditions on the yield of isopropyl chloroacetate. Chloroacetic acid was reacted with isopropanol to produce isopropyl chloroacetate with $Ce(SO_4)_2{\cdot}4H_2O$ as catalyst. The reaction time, the molar ratio of chloroacetic acid to isopropanol and the amount of $Ce(SO_4)_2{\cdot}4H_2O$ were kept to be constants at 4 hours, 1.0:1.3 and 3.5 % of chloroacetic acid weight, respectively. $Ce(SO_4)_2{\cdot}4H_2O$ as the catalyst was reused five times. Table 4 showed the relationship between the yield of isopropyl chloroacetate and the number of $Ce(SO_4)_2{\cdot}4H_2O$ reusing. When $Ce(SO_4)_2{\cdot}4H_2O$ was reused 5 times, the yield of isopropyl chloroacetate still kept at above 92.0 %, so $Ce(SO_4)_2{\cdot}4H_2O$ was proved to be the best catalysts.

Table 4. The relationship between the yield of isopropyl chloroacetate and the number of recycling of $Ce(SO_4)_2{\cdot}4H_2O$

The number of recycling	1	2	3	4	5
Yield, %	97.90	96.43	96.21	94.64	92.50

CONCLUSION

Based on the above discussion and review, using chloroacetic acid and isopropanol as feedstocks and $Ce(SO_4)_2{\cdot}4H_2O$, $NaHSO_4$ and PCl_3 as catalysts, the effect of the reaction time, the molar ratio of chloroacetic acid to isopropanol, the amount of the catalyst and the number of catalyst reusing on the yields of isopropyl chloroacetate have been discussed. The experimental results obtained are the following:

(1) The maximum yield of isopropyl chloroacetate reached at 98.62% in 4 h by the addition of $Ce(SO_4)_2{\cdot}4H_2O$.

(2) The maximum yield of isopropyl chloroacetate reached at 82.4% at chloroacetic acid/isopropanol ratio=1.0:1.2 when $NaHSO_4$ used as the catalyst

(3) The maximum yield of isopropyl chloroacetate was proved to be 89.5% when the amount of used PCl_3 catalyst was 6.7 % of chloroacetic acid weight.

(4) The maximum yield of isopropyl chloroacetate was still kept 92.50% even after 5 recycling of $Ce(SO_4)_2{\cdot}4H_2O$ catalyst.

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