Chinese J. Chem. Eng., **11** (5) 608 – 610 (2003)
RESEARCH NOTES

The Preparation of 2-Chloro-5-chloromethylpyridine in an Airlift Loop Reactor*

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Abstract A new process for the direct chlorination of 2-chloro-5-methylpyridine to yield 2-chloro-5-chloromethylpyridine in an airlift loop reactor (ALR) has been studied. Five main reaction conditions including T_R, n_a/n_s, c_p, Q_g and d_D/d_R were optimized. The average molar yield and purity of 2-chloro-5-chloromethylpyridine obtained were 79% and 98.5% respectively under the optimum operating conditions. Finally, the efficiency for the preparation of 2-chloro-5-chloromethylpyridine with ALR and stirred tank reactor (STR) respectively was compared.
Keywords 2-chloro-5-chloromethylpyridine, 2-chloro-5-methylpyridine, direct chlorination, airlift loop reactor

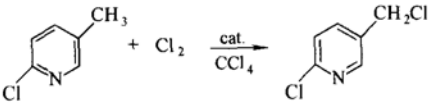
1 INTRODUCTION

Fruit flies are serious problems for agriculture industry and cause extensive damage to crops. A variety of methods have previously been utilized in efforts to control fruit flies. Imidacloprid and acetamiprid have been proved to be two of the safe and high efficient pesticide compounds[1,2]. 2-Chloro-5-chloromethylpyridine is the important intermediate for producing them. There are several methods to prepare 2-chloro-5-chloromethylpyridine, including 2-chloro-5-methylpyridine method[3,4], niacin method[5] and 3-methylpyridine method[6]. Among them, the synthesis of 2-chloro-5-methylpyridine with chlorine gas with catalyst to directly prepare 2-chloro-5-chloromethylpyridine in the STR was one of the most simple, effective and economical methods. None is known, however, about the process for the direct chlorination of 2-chloro-5-methylpyridine to yield 2-chloro-5-chloromethylpyridine with multiphase flow reactors suitable for a large number of the gas-liquid two-phase and the gas-liquid-solid three-phase heterogeneous chemical reaction systems. The ALR, characterized by a well defined flow pattern with effective dispersing effect, relatively low power consumption and high mass transfer coefficient, is being widely used for multiphase chemical reactions[7–9]. The aim of the present study was both to develop ALR and to obtain the optimum operating conditions for the direct chlorination of 2-chloro-5-methylpyridine to yield 2-chloro-5-chloromethylpyridine.

2 EXPERIMENTAL

2.1 Method of synthesis

It is known the side chain of 2-chloro-5-methylpyridine can react using azobisisobuty ronitrile as catalyst, with chlorine gas, to have one hydrogen atom being substituted by chlorine atom, and the product of 2-chloro-5-chloromethylpyridine is obtained. The synthetic route is outlined below



2.2 Experimental setup

The experimental setup used to prepare 2-chloro-5-chloromethylpyridine is schematically shown in Fig. 1. Five 0.7 m long glass draft tubes of 0.05, 0.06, 0.07, 0.08 and 0.09 m inside diameter were fixed concentrically inside the 1.0m long glass reactor tube of 0.1 m inside diameter, respectively. The d_D/d_R ratios obtained: 0.5, 0.6, 0.7, 0.8 and 0.9 respectively and the work volume of the ALR was 7.85 L. A concentric jet nozzle with diameter of 0.003 m was designed and was located at the bottom part of the draft tube. Chlorine and nitrogen gas supplied with gas storage tanks

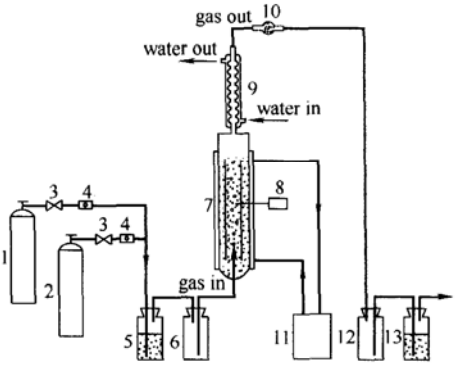


Figure 1 Experimental setup
1—N_2 cylinder; 2—Cl_2 cylinder; 3—stopvalve; 4—flowmeter; 5—drying bottle; 6—gas buffer bottle; 7—ALR; 8—temperature measurement system; 9—condenser tube; 10—drying tube; 11—thermostatic bath; 12—gas buffer bottle; 13—absorption bottle

Received 2002-11-15, accepted 2003-05-29.
* Supported by the Natural Science Foundation of Tianjin (No. 013605711) and the National Natural Science Foundation of China (No. 20176040).
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entered into the draft tube to circulate the solution inside the reactor. The gas flowrate was controlled by calibrated rotameter. The excess chlorine gas and the produced hydrogen chloride by the reaction were absorbed by sodium hydroxide solution. Temperature controlling system maintained a constant reaction temperature. Condenser connected at the outlet of the ALR kept condensation and circumfluence of the reaction mixture stream. In order to protect the reaction system from absorbing water, drying tube containing anhydrous calcium chloride and drying bottle containing concentrated sulfuric acid were connected to the inlet and outlet of this reactor, respectively.

2.3 Synthetic process

The preparation of 2-chloro-5-chloromethylpyridine was performed as follows: into the ALR, 2-chloro-5-methylpyridine, azobisisobutyronitrile and 6 L carbon tetrachloride were added and mixed thoroughly by continuously feeding nitrogen gas, and then the reaction mixture were heated up to boiling point by thermostatic bath. After stop feeding nitrogen gas, the dried chlorine gas was introduced into the solution in the reactor with gas chromatograph detecting the content of 2-chloro-5-chloromethylpyridine and 2-chloro-5-dichloromethylpyridine as the byproduct. Chlorine gas was terminated when the content of the byproduct had been found to reach 0.5%—1%. Later, the nitrogen gas was introduced into the reactor again to blow away the excess chlorine gas and hydrogen chloride produced in the reaction.

The reaction mixture was introduced into a 10 L distillation still with pH adjusted to 6 with 40%(by mass) potassium carbonate solution and then the aqueous phase was removed after phase separation. The organic layer obtained was distilled under high vacuum. Carbon tetrachloride, 2-chloro-5-methylpyridine, 2-chloro-5-chloromethylpyridine were separated gradually. The unreacted 2-chloro-5-methylpyridine can be used in the next synthetic process.

The purity and structure of 2-chloro-5-chloromethylpyridine were detected by gas chromatograph and analyzed by ^{1}H-NMR, respectively. The purity of the final product is higher than 98.5% and the analyzed result of ^{1}H-NMR ($CDCl_3$, 200 MHz, δ ppm) is 8.37 (s, 1H), 7.24—7.67 (m, 2H) and 4.54 (s, 2H).

3 RESULTS AND DISCUSSION

Reaction temperature is a key factor for chemical reaction and the increasing of temperature will speed up the reaction rate remarkably. As can be seen from Fig. 2, a highest molar yield of product was obtained at 75—80℃ which is very close to the boiling point of the reaction mixture. On the other hand, the effect of boiling on the mass transfer may be another factor on the increasing of the molar yield.

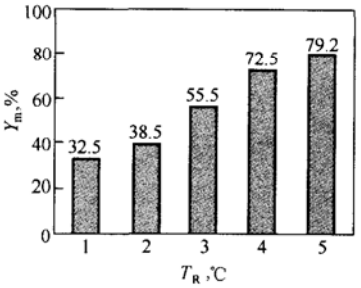

Figure 2 Effect of reaction temperature on the molar yield of 2-chloro-5-chloromethylpyridine
(n_a/n_s=0.08, c_p = 0.5 g·ml^{-1}, Q_g = 40 L·h^{-1}, d_D/d_R = 0.70)
1—55—60℃; 2—60—65℃; 3—65—70℃; 4—70—75℃; 5—75—80℃

The influence of n_a/n_s on the molar yield of 2-chloro-5-chloromethylpyridine is shown in Fig. 3. It is clear that when n_a/n_s varies from 0.02 to 0.06, the yield of 2-chloro-5-chloromethyl pyridine has increased with an increase in n_a/n_s. When n_a/n_s is higher than 0.06, the yield of 2-chloro-5-chloromethylpyridine is insensitive to the n_a/n_s ratio, and with waste of the azobisisobutyronitrile as catalyst. Therefore the optimum n_a/n_s can be selected as 0.06.

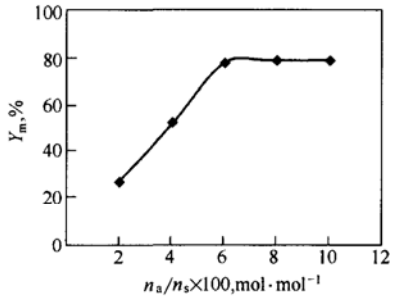

Figure 3 Effect of n_a/n_s on the molar yield of 2-chloro-5-chloromethylpyridine
(T_R = 75—80℃, c_p = 0.5 g·ml^{-1}, Q_g = 40 L·h^{-1}, d_D/d_R =0.70)

The typical effect of the concentration of 2-chloro-5-methylpyridine on the molar yield of 2-chloro-5-chloromethylpyridine is illustrated in Fig. 4. It is found that the conversion rate of 2-chloro-5-methylpyridine decreased slightly with the increase in c_p and the optimum concentration of 2-chloro-5-methylpyridine can be selected as 0.5 g·ml^{-1}.

As can be seen from Fig. 5, the molar yield of 2-chloro-5-chloromethylpyridine increased with an increase in the chlorine gas flowrate. The optimum chlorine gas flowrate can be considered selected as 35 L·h^{-1}.

Figure 6 shows the effect of d_D/d_R on the molar yield of 2-chloro-5-chloromethylpyridine. The maximum molar yield of 2-chloro-5-chloromethylpyridine was obtained at 0.70 of d_D/d_R. It may be attributed

to the largest overall gas-liquid volumetric mass transfer coefficient among the range of the d_D/d_R studied.

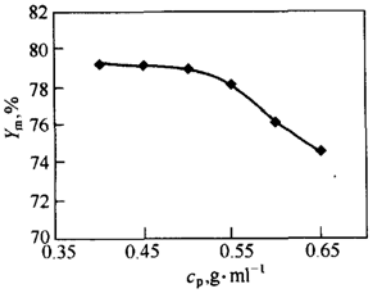

Figure 4 Effect of concentration of 2-chloro-5-methylpyridine on the molar yield of 2-chloro-5-chloromethylpyridine
(T_R = 75—80℃, n_a/n_s = 0.08, Q_g = 40 L·h^{-1}, d_D/d_R =0.70)

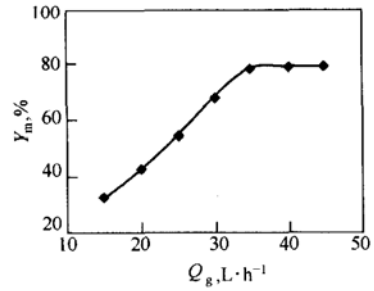

Figure 5 Effect of chlorine gas flowrate on the molar yield of 2-chloro-5-chloromethylpyridine
(T_R = 75—80℃, n_a/n_s = 0.08, c_p = 0.5 g·ml^{-1}, d_D/d_R =0.70)

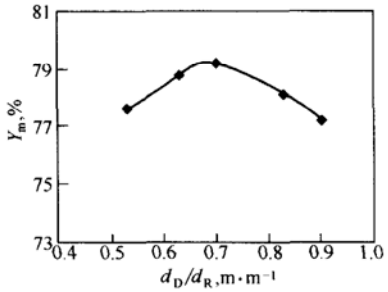

Figure 6 Effect of d_D/d_R on the molar yield of 2-chloro-5-chloromethylpyridine
(T_R = 75—80℃, n_a/n_s = 0.08, Q_g = 40 L·h^{-1}, c_p = 0.5 g·ml^{-1})

The stability of experimental result was carried out at T_R = 75—80℃, n_a/n_s = 0.06, Q_g = 35 L·h^{-1}, c_p = 0.5 g·ml^{-1}, d_D/d_R = 0.70. As can be seen from Fig. 7, under the above optimum operating conditions the average molar yield and purity of 2-chloro-5-chloromethylpyridine are higher than 79% and 98.5% respectively for ten times of experiments.

As can be calculated from Table 1, the molar yield of 2-chloro-5-chloromethylpyridine has increased by 4.49%, the reaction time has decreased by 21.7% and the quantity of chlorine gas has decreased by 29.9% in the ALR with d_D/d_R=0.70 relatively to that in STR under the operating conditions such as T_R = 75—80℃, n_a/n_s = 0.08, Q_g = 38.5 L·h^{-1}, c_p = 0.5 g·ml^{-1}. It may be due to the higher gas-liquid mass transfer and the longer gas residence time in the ALR.

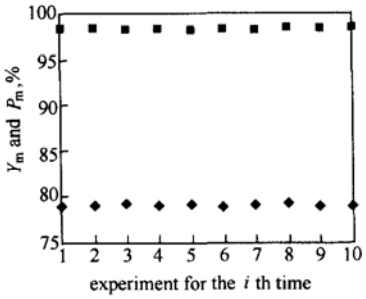

Figure 7 Stability of the molar yield and purity under the optimum operating conditions
(T_R = 75—80℃, n_a/n_s = 0.06, Q_g = 35 L·h^{-1}, c_p = 0.5 g·ml^{-1}, d_D/d_R = 0.70)
■ P_m; ◆ Y_m

Table 1 Comparison of economical efficiency of ALR to that of STR

Reactor	Y_m, %	P_m, %	Reaction time, h	Quantity of chlorine gas used, L
ALR	79.2	98.52	1.8	62.1
STR	75.8	98.5	2.3	88.6

NOMENCLATURE

c_p	concentration of 2-chloro-5-methylpyridine, g·ml^{-1}
d_D	inside diameter of draft tube, m
d_R	inside diameter of reactor, m
n_a	mole number of azobisisobutyronitrile, mol
n_s	mole number of 2-chloro-5-methylpyridine, mol
P_m	purity of 2-chloro-5-chloromethylpyridine, %
Q_g	chlorine gas flowrate, L·h^{-1}
T_R	reaction temperature, ℃
Y_m	molar yield of 2-chloro-5-chloromethylpyridine, %

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