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The preparation of 2-chloro-5-methyl-pyridine in airlift loop reactor

Wen Jianping*, Wang Changlin, Qiao Ping

School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, PR China

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Abstract

A new process for the direct chlorination of 3-methyl-pyridine with special catalyst to yield 2-chloro-5-methyl-pyridine in the airlift loop reactor has been considered. The effects of reaction temperature, the molar ratio of palladium chloride to 3-methyl-pyridine, concentration of 3-methyl-pyridine, chlorine gas flowrate and the ratio of the inside diameter of the draft tube to that of the reactor on the molar yield of 2-chloro-5-methyl-pyridine were investigated and discussed, and an optimum operation condition was found. The average molar yield of 2-chloro-5-methyl-pyridine comes up to 60% under the optimum operation condition.

Keywords: 2-Chloro-5-methyl-pyridine; 3-Methyl-pyridine; Direct chlorination; Airlift loop reactor

1. Introduction

2-Chloro-5-methyl-pyridine is an important intermediate for producing high efficient, low residual pesticides such as imidacloprid, acetamiprid, etc. Study on the synthesis of it has received much attention in last 20 years. There are various methods to synthesize 2-chloro-5-methyl-pyridine, including oxidation method [1–5], eyclocondensation method [6–8], diazotization method [9–11], melting salt method [12], cyclization method [13–17], pyridone method [18]. In all these methods exist some different disadvantages. A new synthetic reaction of 3-methyl-pyridine with chlorine under the special catalyst to directly prepare 2-chloro-5-methyl-pyridine has been reported [19]. None is known, however, about the process for the direct chlorination of 3-methyl-pyridine to yield 2-chloro-5-methyl-pyridine in the multiphase flow reactors suitable for a large number of chemical reactions for gas–liquid two-phase and gas–liquid–solid three-phase heterogeneous systems. The airlift loop reactors [20], characterized by a well defined flow pattern, better dispersing effects, relatively low power consumption and a higher mass transfer coefficient, are widely used in multiphase chemical reactions [21,22]. The aim of the present study was both to develop the airlift loop reactor and to obtain the optimum operation conditions for the direct chlorination of 3-methyl-pyridine to yield 2-chloro-5-methyl-pyridine.

* Corresponding author. Tel.: +86-22-2740-1664; fax: +86-22-2350-1622.
E-mail address: jpwen@tju.edu.cn (W. Jianping).

2. Experimental

2.1. Principle of synthesis

3-Methyl-pyridine and palladium chloride were used as the starting material and the catalyst, respectively. 2-Chloro-5-methyl-pyridine could be obtained directly through the synthetic reaction of 3-methyl-pyridine with chlorine. The synthetic route was outlined in Scheme 1.

2.2. Experimental setup

The experimental setup used to prepare 2-chloro-5-methyl-pyridine is schematically shown in Fig. 1. Five 0.24 m high glass draft tubes of 0.016, 0.019, 0.021, 0.025, 0.027 m inside diameter were fixed concentrically inside the main 0.30 m high glass reactor tube of 0.03 m inside diameter, respectively. Correspondingly, the ratio of the inside diameter of the draft tube to that of the reactor contained 0.53, 0.63, 0.70, 0.83, 0.9, and the work volume of the reactor was 250 cm^3. A concentric jet nozzle with the diameter of 1.6 mm was designed and was located in the bottom part of the riser. The gas flowrate was controlled by calibrated rotameter. In order to protect the reaction system from absorbing water, drying tube containing anhydrous calcium chlorine and drying bottle containing concentrated sulfuric acid were connected to the inlet and outlet of this reactor, respectively. The extra chlorine gas of this reaction was absorbed by sodium hydroxide. Temperature controlling system maintained a constant temperature of reaction. Chlorine and ni-

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Nomenclature

C_p	concentration of 3-methyl-pyridine (g/cm^3)
d_D	inside diameter of draft tube (m)
d_R	inside diameter of reactor (m)
v	gas flow capacity (cm^3/min)
n_{PdCl_2}	mole number of palladium chloride (mol)
$n_{C_6H_7N}$	mole number of 3-methyl-pyridine (mol)
Q_g	chlorine gas flowrate (cm^3/s)
T_R	reaction temperature (°C)
Y_m	molar yield of 2-chloro-5-methyl-pyridine (dimensionless)

trogen gas supplied with a gas storage tank entered into the riser, pushed the solution to circulate inside this reactor.

2.3. Synthesis process

The synthesis of 2-chloro-5-methyl-pyridine was performed as follows: in the airlift loop reactor, 3-methyl-pyridine, palladium chloride and 200 cm^3 carbon tetrachloride were added and mixed thoroughly by continuously feeding nitrogen gas, and then were heated to 70 °C within 1 h by thermostatic bath. The solution became reddish gradually and the acquired mixture was heterogeneous. The mixture was continuously kept at 70 °C for 30 min with feeding nitrogen gas, and then cooled to room temperature by low temperature trough. The solution became shallow yellow and the mixture became homogeneous. The reaction system was further cooled by low temperature trough. After ceasing nitrogen gas, the dried chlorine gas was introduced into the above solution of this reactor for 30 min and the solution became brownish red. The mixture was then warmed up to room temperature about 25 °C and kept it for 12 h by thermostatic bath.

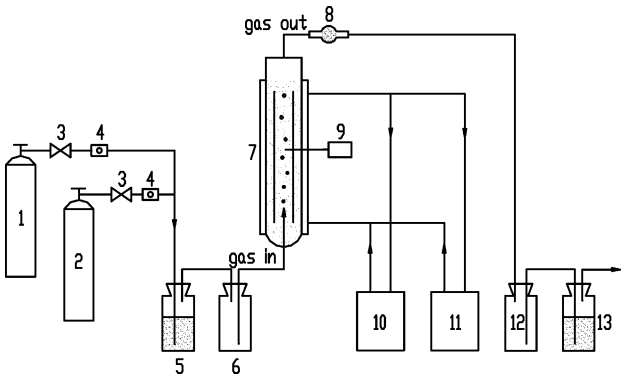
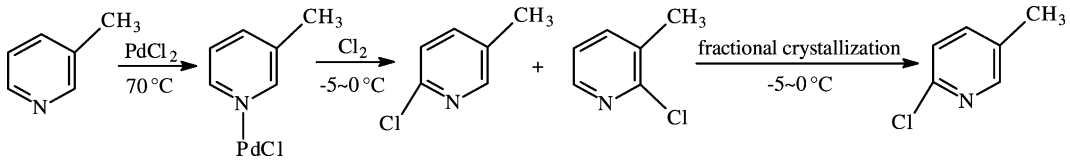


Fig. 1. Experimental setup: 1, N_2 cylinder; 2, Cl_2 cylinder; 3, stopvalve; 4, flowmeter; 5, drying bottle; 6, gas buffer bottle; 7, airlift loop reactor; 8, drying tube; 9, temperature measurement system; 10, thermostatic bath; 11, low temperature trough, 12, gas buffer bottle; 13, absorption bottle.

This mixture was introduced into the 500 cm^3 four-port flask and alkalified to pH = 6 with 40% sodium hydroxide and then distilled with water vapor, a colorless solution was obtained. The organic layer was separated and the aqueous layer was further extracted with carbon tetrachloride (30 cm^3 × 3). The carbon tetrachloride layer and organic layer were combined and dried over anhydrous magnesium sulfate. Carbon tetrachloride was removed under reduced pressure distillation. The product was further fractionally crystallized at −5 to 0 °C to give a colorless oil liquid. The molar yield of 2-chloro-5-methyl-pyridine can be calculated with the weight of the final product.

2.4. Detecting method

The purity and structure of 2-chloro-5-methyl-pyridine 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 7.192–8.205 (m, 3H) and 2.306 (S, 3H).



Scheme 1. structural formula and synthetic route of 2-chloro-5-methyl-pyridine.

Table 1
The detecting conditions of gas chromatograph

Analyzer type	Supporting medium	Immobile liquid	Detector	Chromatographic column	
GC-7890F	880 white silanizing monomer	Polyethylene glycol (20 M)	Hydrogen flame	Stainless steel column 3000 mm × 2 mm	
Column temperature (°C)	Gasifying temperature (°C)	Detecting temperature (°C)	Carrier gas	Flow capacity (cm^3/min)	Sample size (μl)
110	210	235	Nitrogen	v_{N_2} = 35, v_{H_2} = 35, v_{air} = 350	0.2

Table 2
The working conditions of ^{1}H-NMR

Working frequency (MHz)	Working temperature (°C)	Solvent
200	25	Methenyl chloride

The detecting conditions of gas chromatograph were listed in Table 1.

The working conditions of ^{1}H-NMR were listed in Table 2.

3. Experimental results and discussion

3.1. Effect of reaction temperature

Temperature is an important affecting factor toward reaction rate and reaction equilibrium. This reaction occurs at lower temperature and higher yield of 2-chloro-5-methyl-pyridine was obtained at the optimum reaction temperature of −5 to 0 °C as shown in Fig. 2.

3.2. Effect of $n_{PdCl_2}/n_{C_6H_7N}$

The influence of $n_{PdCl_2}/n_{C_6H_7N}$ on the molar yield of 2-chloro-5-methyl-pyridine at the fixed reaction temperature, chlorine gas flowrate, concentration of 3-methyl-pyridine and the ratio of the inside diameter of the draft tube to that of the reactor (d_D/d_R) is shown in Fig. 3. It is clear that when $n_{PdCl_2}/n_{C_6H_7N}$ varies from 0.01 to 0.08, the yield of 2-chloro-5-methyl-pyridine has increased with an increase in the $n_{PdCl_2}/n_{C_6H_7N}$. And when the $n_{PdCl_2}/n_{C_6H_7N}$ is larger than 0.08, the yield of 2-chloro-5-methyl-pyridine is insensitive to the $n_{PdCl_2}/n_{C_6H_7N}$, and resulting in the waste of the palladium chloride catalyst. Therefore, the optimum $n_{PdCl_2}/n_{C_6H_7N}$ was selected as 0.08.

3.3. Effect of concentration of 3-methyl-pyridine

The typical results of the yield of 2-chloro-5-methyl-pyridine as a function of the concentration of 3-methyl-pyridine are illustrated in Fig. 4. It is found that the yield of 2-chloro-5-methylpyridine decreased slightly with the increase in the C_p and the output of 2-chloro-5-methyl-pyridine increased accordingly for the C_p small than 0.16 g/cm^3, however decreased remarkably with increasing in the C_p for the C_p higher than 0.16 g/cm^3. This is due to the increase in the yield of 2-chloro-3-methyl-pyridine as byproduct on the basis of the result detected by the gas chromatograph. The optimum concentration of 3-methyl-pyridine was selected as 0.16 g/cm^3.

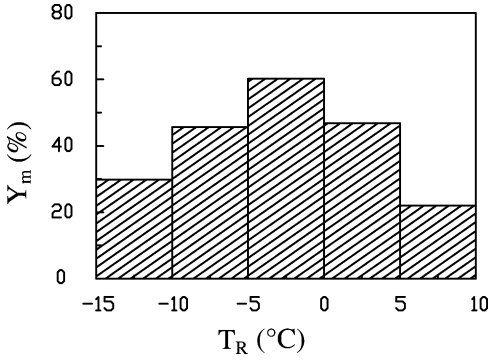


Fig. 2. Effect of reaction temperature on molar yield ($n_{PdCl_2}/n_{C_6H_7N}$ = 0.1, C_p = 0.15 g/cm^3, Q_g = 1.96 cm^3/s, d_D/d_R = 0.7).

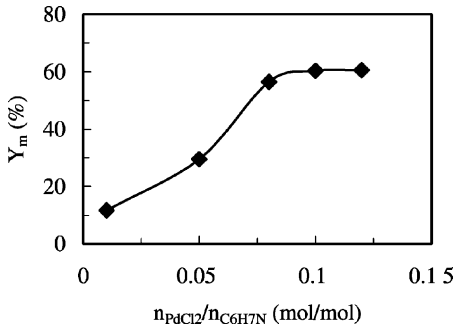


Fig. 3. Effect of $n_{PdCl_2}/n_{C_6H_7N}$ on molar yield (T_R = −5 to 0 °C, C_p = 0.15 g/cm^3, Q_g = 1.96 cm^3/s, d_D/d_R = 0.70).

3.4. Effect of chlorine gas flowrate

As it can be seen from Fig. 5, the yield of 2-chloro-5-methyl-pyridine increased with increasing in the chlorine gas flowrates. It was mainly explained by the fact that the increasing in chlorine gas flowrates brings about the increase of the gas holdup, the decrease of the bubble diameter, the increases of the gas–liquid interfacial area and the overall gas–liquid volumetric mass transfer coefficient, and thus causing the increase in the yield of 2-chloro-5-methyl-pyridine. However, the chlorine gas flowrate higher than 1.4 cm^3/s will lead to the waste of the chlorine gas. The optimum chlorine gas flowrate was selected as 1.4 cm^3/s.

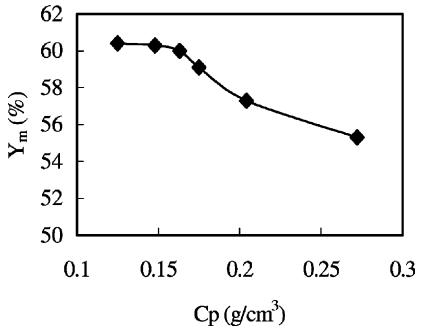


Fig. 4. Effect of concentration of 3-methyl-pyridine on molar yield (T_R = −5 to 0 °C, $n_{PdCl_2}/n_{C_6H_7N}$ = 0.1, Q_g = 1.96 cm^3/s, d_D/d_R = 0.70).

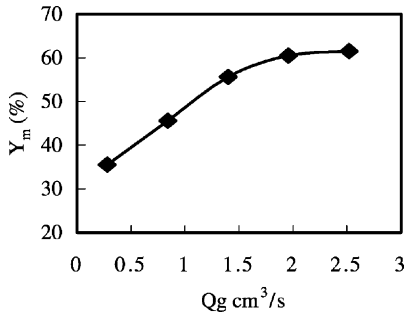


Fig. 5. Effect of chlorine gas flowrate on molar yield ($T_R = -5$ to $0\,^\circ$C, $n_{PdCl_2}/n_{C_6H_7N} = 0.1$, $C_p = 0.15\,g/cm^3$, $d_D/d_R = 0.70$).

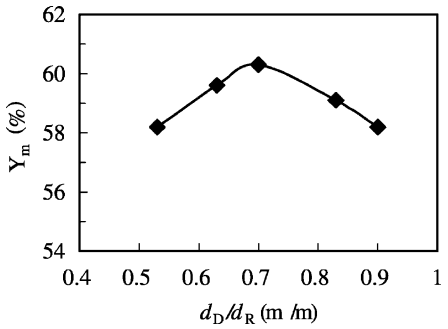


Fig. 6. Effect of d_D/d_R on molar yield ($T_R = -5$ to $0\,^\circ$C, $n_{PdCl_2}/n_{C_6H_7N} = 0.1$, $Q_g = 1.96\,cm^3/s$, $C_p = 0.15\,g/cm^3$).

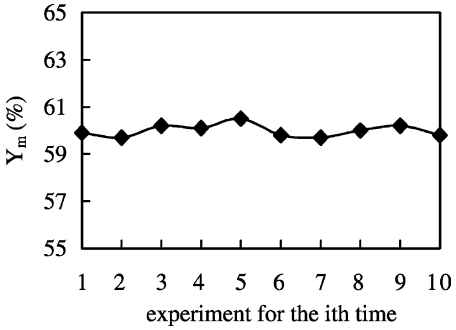


Fig. 7. Stability of the molar yield under the optimum operation conditions.

3.5. Effect of d_D/d_R

Fig. 6 shows the effect of d_D/d_R on the molar yield of 2-chloro-5-methyl-pyridine. The maximum molar yield of 2-chloro-5-methyl-pyridine was obtained at 0.70 of d_D/d_R as shown in Fig. 6. It may be attributed to the largest overall gas–liquid volumetric mass transfer coefficient among the range of the d_D/d_R studied.

3.6. Stability observation under the optimum operation conditions

The experiment was carried out at $T_R = -5$–$0\,^\circ$C, $n_{PdCl_2}/n_{C_6H_7N} = 0.08$, $Q_g = 1.4\,cm^3/s$, $C_p = 0.16\,g/cm^3$, $d_D/d_R = 0.70$. As it can be seen from Fig. 7, under the above optimum operation conditions the average molar yield of 2-chloro-5-methyl-pyridine comes up to 60% for 10 times.

4. Conclusions

A new process for the production of 2-chloro-5-methyl-pyridine by direct chlorination of 3-methyl-pyridine in airlift loop reactor has been considered. The optimum operation conditions of 250 cm^3 airlift loop reactor for preparation of 2-chloro-5-methyl-pyridine are listed as follows: the reaction temperature is -5 to $0\,^\circ$C, the molar ratio of palladium chloride and 3-methyl-pyridine is 0.08, the concentration of 3-methyl-pyridine is 0.16 g/cm^3, the chlorine gas flowrate is 1.4 cm^3/s, and the ratio of the cross-sectional area of the riser to that of this reactor is 0.7. Under the optimum operation conditions, the average molar yield of 2-chloro-5-methyl-pyridine comes up to 60%.

Acknowledgements

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References

[1] G. Bernd, K.H. Joachim, US 4897488 (1990).
[2] K. Dieter, G. Bernd, US 5010201 (1991).
[3] K. Dieter, J. Claus, B. Rudolf, R. Winfried, EP 0438691, 1991.
[4] J. Claus, K. Dieter, G. Bernd, L. Beinhard, DE 4020053, 1991.
[5] J. Claus, K. Dieter, US 5099025 (1992).
[6] L. Reinhard, EP 0546418, 1993.
[7] J. Klaus, L. Hans, M. Christoph, L. Reinhard, M. Walter, US 5648495 (1997).
[8] M. Walter, S. Hermann, M. Christoph, S. Dimitry, DE 19539074, 1997.
[9] S. Ulrich, S. Guido, H. Monika, DE 4005115, 1991.
[10] C. Gunther, L. Hans, DE 4111214, 1992.
[11] C. Gunther, L. Hans, S. Guido, DE 4111215, 1992.
[12] R. Christian, S. Reinhard, W. Helmut, T. Hans-Joachim, DE 4320827, 1995.
[13] W.M. Kruse, J.F. Stephen, US 4645839 (1987).
[14] K. Helmut, US 5466800 (1995).
[15] K. Helmut, K. Alexander, F. Hauke, US 5420284 (1995).
[16] R. Murugan, E.F.V. Scriven, T.Y. Zhang, US 5508410 (1996).
[17] H.L. Albert, S.J. Fergus, EP 0162464, 1985.
[18] R. Osborne, K.D. Bailey, US 4612377 (1986).
[19] Q. Ping, W. Jianping, Modern Chem. Ind. 21 (12) (2001) 23–26.
[20] J. Xinzhen, et al., Theory and Application of Gas–Liquid Reaction, Hydrocarbon Process, Beijing, 1989.
[21] J.A. Orejas, Chem. Eng. Sci. 56 (2001) 513–522.
[22] J.A. Orejas, Chem. Eng. Sci. 54 (1999) 5299–5309.