

Separation of picolines by dissociation extraction

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Abstract: The separation of the by-product (The volume fraction of 3-picoline is 68.472 2% and 4-picoline 26.517 6%.) in the synthesis of pyridine by dissociation extraction was studied. Six separation conditions of the dissociation extraction—the kind and the dosage of extractant and organic solvent, the concentration of the extractant and separation temperature—were investigated. Different levels of each factor were chosen to form an orthogonal test of six factors and five levels. The results show that the volume ratio of 3-picoline and 4-picoline in organic phase is the highest when 24 mL picolines are separated at 0 °C by 2.0 mol/L p-toluenesulfonic and n-heptane whose dosages are 40 mL and 48 mL, respectively. The effect of the separation is considerably improved with repetition test. This process of dissociation extraction has commendable potential for industrial exploitation.

Key words: 3-picoline; 4-picoline; separation; dissociation extraction; orthogonal test

A mixture of 3-picoline and 4-picoline can be obtained in the gas phase synthesis of pyridine by ammonia and aldehyde or ketone. And the mixture's composition changes with the dosage ratio of the raw materials easily. Both 3-picoline and 4-picoline are important raw organic chemicals to produce many fine chemicals with high appended value^[1], such as vitamin B, niacin and isonicotinic acid, etc. Also required by environmental protection, these mixtures should be separated to get the single picoline.

The two picolines are close-boiling-point isomers (144.14 °C, 145 °C^[1], respectively) with similar properties. They are difficult to separate with traditional methods. Presently what can be bought in the domestic market is generally from Japan or USA and the prices are quite high. So it is economical to divide them and take the single product with higher purity to fill the urgent demand at home and abroad.

Dissociation extraction is a form of chemical exchange process in which the difference of the dissociation constants of the components in a mixture is exploited to effect a separation^[2]. It is particularly useful for the separation of closely related compounds or isomers. While 3- and 4-picoline have boiling points differing by only a fraction of a degree, the distinction in molecular arrangements of the two isomers results in an appreciable variation in the dissociation constants (4.54×10^{-9} for 3-picoline as against 10.62×10^{-9} for 4-picoline^[1]). If a solution of the two bases in an organic solvent is contacted with an aqueous phase containing a stoichiometric deficiency of an

acid, the extractant, in relation to the bases in the system, then the two isomers will compete for the available acid. The isomer with the higher dissociation constant, that is the stronger base (4-picoline), will react preferentially with the extractant forming a salt in the aqueous phase, thus causing an enrichment of the organic phase with respect to the weaker base (3-picoline). If this principle is extended to a multi-stage counter-current operation then products of high purity can be obtained^[3,4].

1 Research Objects

Six factors were selected as research objects to get the optimum separation conditions on the basis of the whole process.

1) Extractant The total process consists of the dissociation extraction of the mixtures, the separation of 3-picoline and the organic solvent, the decomposition of the salt and the postprocessing in the aqueous phase. Proper extractant should take the competition reaction to be fully performed and is vitally important to the separation. It can decrease the distance of the distribution coefficients so as to improve the separation factor. Because the dosage of the extractant and the consumption of energy result in the major operation cost, the extractant should be easily refreshable as well.

2) Organic solvent The organic solvent should be water-immiscible. It is better for its boiling point not to exceed 100 °C because of the requirement to reduce the consumption of energy. The solvent can change distribution coefficients of the extraction equilibrium. When the difference of the dissociation constants is not enough to effect the separation, changing the organic solvent is one of the feasible methods. The influence of the organic solvent is related to its acting

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force on each component.

3) Concentration of the extractant In a certain range of concentration the increase of the concentration of the extractant will decrease the dissociation constants of the picolines. On the other hand, the probability of the competition reaction will rise with higher concentration, which will affect the dissociation equilibrium and enlarge the difference of the dissociation constants. In consideration of the saturated solubility of each extractant, five levels like 1 mol/L, 2 mol/L and so on were chosen.

4) Addition of the extractant The addition of a neutralizing agent in stoichiometric deficient amount is the key of the dissociation extraction. The average dosage of the extractant was about 58.5 mL, so five levels from 10 to 80 mL were chosen.

5) Addition of the organic solvent According to

the basic extraction theory, the concentration of 3-picoline in organic phase increases with the addition of the organic solvent so as to improve the distribution coefficient. But this increase effect has a high point and the amount of organic solvent causes the main consumption of energy in after-treatments. Therefore, it is necessary to find out the optimal addition and five different additions of the organic solvent with 1.5 to 5 times to that of the picolines were selected.

6) Separation temperature There are two ways for the temperature to impact the separation. On the one hand, the higher the temperature is, the quicker the competition exchange takes place. On the other hand, the increase of the temperature can restrain the dissociation of the picolines in the aqueous phase.

Five levels of each factor above are picked out as research objects and shown in Tab. 1.

Tab. 1 Research objects

Level	Factor					
	Extractant	Concentration of extractant/(mol·L ⁻¹)	Volume of extractant/mL	Organic solvent	Volume of organic solvent/mL	Separation temperature/°C
1	Hydrochloric acid (A1)	1(B1)	10(C1)	Benzene (D1)	36(E1)	25(F1)
2	Acetic acid (A2)	2(B2)	20(C2)	Toluene (D2)	48(E2)	0(F2)
3	P-toluenesulfonic acid (A3)	4(B3)	40(C3)	N-heptane (D3)	72(E3)	-10(F3) ^[5]
4	Sodium biphosphate(A4)	5(B4)	60(C4)	Phenixin (D4)	96(E4)	-10(F4) ^[5]
5	Benzoic acid (A5)	6(B5)	80(C5)	Dichloromethane (D5)	120(E5)	-10(F5) ^[5]

2 Experiment

2.1 Materials

The isomers were obtained from Red Sun Group Co., Ltd. They are the by-product of the synthesis of pyridine and found out to contain 68.472 2% (volume fraction) 3-picoline and 26.517 6% 4-picoline. Different organic solvents, namely, benzene, n-heptane, toluene, etc. were of analytic grade. The extractants, like hydrochloric acid, acetic acid and sodium biphosphate were of analytic grade as well, while the p-toluenesulfonic acid and benzoic acid used were of chemical grade. Distilled water was used for making up the aqueous phase of appropriate concentration. The purities of all organic compounds were checked by gas-liquid chromatography (GLC).

2.2 Separation of the picolines

A known weight of extractant in stoichiometric deficiency was added to the mixture of the bases. The mixture was vigorously stirred at constant temperature for 5 h after which the system came to the balance. The organic compounds were extracted from the solution by a water-insoluble organic solvent, e. g., n-heptane. The volume of the organic solution was measured. And the volume fraction of undissociated base in organic phase was detected by GLC. The specific operation conditions of each experiment were described in detail in Tab. 2. The operation conditions of GLC

came from Ref. [6].

3 Results and Analysis

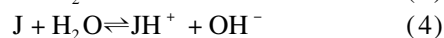
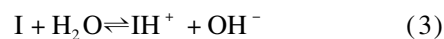
The overall distribution coefficients of the individual bases are given by

$$D'_I = \frac{C_{I,s}}{C_{I,a} + C_{IH^+,a}} \quad (1)$$

$$D'_J = \frac{C_{J,s}}{C_{J,a} + C_{JH^+,a}} \quad (2)$$

where C are the mol concentrations of the species indicated; I and J represent 3-picoline and 4-picoline correspondingly; IH^+ and JH^+ represent the dissociated 3-picoline and 4-picoline in aqueous phase, respectively; the subscript a means the aqueous phase and s the organic phase. This equation assumes the picoline salt to be fully ionized in the aqueous phase. At the same time it is suggested that all the activity coefficients are unconsidered because the two bases are isometric. The activity coefficient of IH^+ and undissociated I should be approximately equal to that of the JH^+ and undissociated J in the same solution.

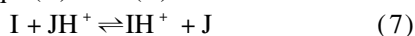
Equilibriums established in the aqueous phase are as follows:



Tab. 2 Operation parameters of the orthogonal test

No.	Extractant	Concentration of extractant/(mol·L ⁻¹)	Volume of extractant/mL	Organic solvent	Volume of organic solvent/mL	Separation temperature/°C
1	A1	1	20	D4	72	0
2	A2	1	80	D5	120	-10
3	A3	1	60	D1	96	25
4	A4	1	10	D3	36	-10
5	A5	1	40	D2	48	-10
6	A1	2	40	D3	96	-10
7	A2	2	20	D2	36	25
8	A3	2	80	D4	48	-10
9	A4	2	60	D5	72	-10
10	A5	2	10	D1	120	0
11	A1	4	10	D5	48	25
12	A2	4	40	D1	72	-10
13	A3	4	20	D3	120	-10
14	A4	4	80	D2	96	0
15	A5	4	60	D4	36	-10
16	A1	5	60	D2	120	-10
17	A2	5	10	D4	96	-10
18	A3	5	40	D5	36	0
19	A4	5	20	D1	48	-10
20	A5	5	80	D3	72	25
21	A1	6	80	D1	36	-10
22	A2	6	60	D3	48	0
23	A3	6	10	D2	72	-10
24	A4	6	40	D4	120	25
25	A5	6	20	D5	96	-10

The base I and J compete for protons and their relative strengths determine the equilibrium position of the following key exchange reaction which is the sum of reactions in Eqs. (5) and (6):



The material balance equations of each base are as follows:

$$n_{I,a} + n_{IH^+,a} = n_{I,0} - n_{I,s} \quad (8)$$

$$n_{J,a} + n_{JH^+,a} = n_{J,0} - n_{J,s} \quad (9)$$

where n is the amount of substance and the subscript 0 is the symbol of the original value. Along with the detection concentration ($y_{I,s}$ and $y_{J,s}$, where y is the volume fraction of undissociated base in organic phase) of the picolines and the volume of the organic phase (V_s). According to Eqs. (8) and (9), the overall distribution coefficients can be calculated as

$$D'_I = \frac{y_{I,s} V_s \rho_I / (M_I V_s)}{(y_{I,0} V_0 \rho_I / M_I - y_{I,s} V_s \rho_I / M_I) / V_a} = \frac{y_{I,s} V_a}{y_{I,0} V_0 - y_{I,s} V_s} \quad (10)$$

$$D'_J = \frac{y_{J,s} V_s \rho_J / (M_J V_s)}{(y_{J,0} V_0 \rho_J / M_J - y_{J,s} V_s \rho_J / M_J) / V_a} = \frac{y_{J,s} V_a}{y_{J,0} V_0 - y_{J,s} V_s} \quad (11)$$

where ρ is the density of organic base and M is the molecular weight of picolines. So the separation factor α in the system, which is given by the ratio of their overall distribution coefficients, should be calculated as

$$\alpha = \frac{D'_I}{D'_J} = \frac{y_{I,s} (y_{J,0} V_0 - y_{J,s} V_s)}{y_{J,s} (y_{I,0} V_0 - y_{I,s} V_s)} \quad (12)$$

And the volume ratio r of 3-picoline and 4-picoline is defined as

$$r = \frac{V_{I,s}}{V_{J,s}} = \frac{y_{I,s}}{y_{J,s}} \quad (13)$$

The calculated volume ratios and separation factors by Eqs. (12) and (13) are shown in Tab. 3. It also gives the detection concentrations $y_{I,s}$ and $y_{J,s}$ and the volume of the organic phase V_s .

The values of r and α matched very well and changed in the same trend that validated the basic principle well. It was absolutely different from Guitar's results in which r and α changed irregularly^[7].

So the value of r can fully represent the achievement of the separation. To simplify the analysis the volume ratio can be used as main index to analyze the results of the orthogonal test shown in Tab. 4, where R is the range.

According to the value of K , the average volume ratio of each factor, the optimum conditions are A3B2C3D3E2F2, namely separated at 0 °C by 2.0 mol/L p-toluenesulfonic and n-heptane whose dosages are 40 mL and 48 mL, respectively. The results also show when p-toluenesulfonic acid is used as the extractant the best ratio of its amount to that of the picolines is 1:2. 925.

Tab.3 Volume ratios and separation factors of the orthogonal test

No.	$y_{I,s}$	$y_{J,s}$	V_s/mL	r	α	No.	$y_{I,s}$	$y_{J,s}$	V_s/mL	r	α
1	0.145 613	0.046 163	80	3.15	1.76	14	0.053 313	0.015 366	112	3.47	1.54
2	0.017 319	0.005 145	138	3.37	1.35	15	0.058 727	0.026 000	55	2.26	0.88
3	0.037 203	0.009 915	118	3.75	1.62	16	①	①	120	①	①
4	0.065 906	0.022 188	32	2.97	1.16	17	0.150 439	0.059 822	107	2.51	2.35
5	0.085 875	0.029 722	72	2.89	1.19	18	0.132 686	0.028 543	35	4.65	2.21
6	0.043 600	0.010 305	105	4.23	1.89	19	0.204 390	0.069 407	59	2.94	1.52
7	0.104 972	0.039 167	36	2.68	1.04	20	0.049 778	0.028 111	54	1.77	0.62
8	0.149 830	0.032 642	53	4.59	2.60	21	0.002 300	0.001 000	41	2.30	0.89
9	0.125 542	0.042 563	96	2.95	1.71	22	0.024 400	0.004 700	52	5.19	2.10
10	0.060 926	0.023 492	122	2.59	1.07	23	0.077 194	0.024 824	86	3.11	1.42
11	0.099 378	0.032 308	65	3.08	1.30	24	0.037 417	0.011 605	117	3.22	1.40
12	0.076 882	0.022 718	85	3.38	1.60	25	0.032 288	0.053 726	102	0.60	0.05
13	0.027 111	0.008 516	126	3.18	1.35						

Note: ① The picolines reacted with the acid completely in this experiment and the concentration of the bases in organic phase were not high enough to be detected.

Tab.4 Direct analysis of the orthogonal test

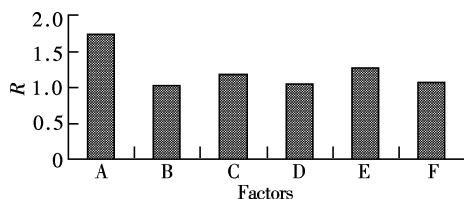
No.	Effect of each factor					
	Extractant (A)	Concentration of extractant (B)	Volume of extractant (C)	Organic solvent (D)	Volume of organic solvent (E)	Separation temperature (F)
K1	2.55	3.23	2.85	2.99	2.97	2.90
K2	3.43	3.41	2.51	2.43	3.74	3.81
K3	3.86	3.07	3.68	3.47	2.87	
K4	2.88	2.38	2.83	3.14	2.91	2.75
K5	2.13	2.89	3.10	2.93	2.47	
R	1.73	1.03	1.17	1.04	1.27	1.06

The optimal parameters were tested by the repetition experiments. The results in Tab. 5 show that the operation values obtained by the orthogonal test are reliable and the process is easily reduplicated.

Tab.5 Volume ratios and separation factors of repetition test

Test	$y_{I,s}$	$y_{J,s}$	V_s/mL	r	α
1	3.884×10^{-2}	7.91×10^{-3}	50	4.91	2.05
2	2.802×10^{-2}	5.76×10^{-3}	50	4.86	2.00

The effect of each factor was also studied by the comparison of the range R . As shown in Fig. 1, the primary factor to the whole process is the kind of extractant, then is the addition of organic solvent, after that is the dosage of extractant, finally are the concentration of extractant, the kind of organic solvent and separation temperature which have almost the same effect on the separation.

**Fig. 1** Comparison of each factor

4 Discussions

4.1 Effect of the amount of extractant

In the process of dissociation extraction the amount of the extractant should be deficient to form

the competition between 3-picoline and 4-picoline. The better separation factor can be obtained if the more 4-picoline reacts with the extractant. In the six experiments with sufficient extractant it was found there were two kinds of results. In the system with stronger acid (hydrochloric acid and benzoic acid) in experiment No. 16, 20 and 21, there was almost nothing in the organic phase and the values of separation factors were very small. In this kind of condition the amount of the extractant should be stoichiometric deficient to that of 4-picoline. While in the weaker acid system (acetic acid, p-toluenesulfonic acid and sodium biphosphate) like experiment No. 14, 22 and 24, although the amount of the extractant was excessive the separation was still performed and the values of separation factors were 1.54, 2.10 and 1.40, respectively. So the stoichiometric deficiency amount is determined by the acidity. The weaker the acid is, the more and, even apparently, excessive dosage of extractant is required.

4.2 Effect of the organic solvent

Not only the difference of dissociation constants between two components but also the distribution coefficients of the solutes in two phases influence the results of dissociation extraction separation. Compared with other close boiling point mixtures, both 3- and 4-picoline are diffuent in water, therefore, the solubility of the organic solvent must be considered in the analysis. The separation factor is greater when n-heptane is employed as an organic solvent rather than benzene

and so on. Benefit accrues if the organic solvent with the lowest solubility in water can be chosen, which can enlarge the distribution of the undissociated bases to favor the separation.

5 Conclusion

Dissociation extraction is a convenient and practical method to separate 3-picoline and 4-picoline, which are difficult to separate by normal methods. The separation of the by-product (The volume fraction of 3-picoline is 68.472 2% and 4-picoline 26.517 6%) in the synthesis of pyridine by dissociation extraction was studied. The results of the orthogonal test show that the volume ratio of 3-picoline and 4-picoline in organic phase is the highest when 24 mL picolines are separated at 0 °C by 2.0 mol/L p-toluenesulfonic and n-heptane whose dosages are 40 mL and 48 mL, respectively.

The sequence of the effect of each factor is as follows: the kind of extractant > the addition of organic solvent > the dosage of extractant > the concentration of extractant, the kind of organic solvent and separation temperature.

When p-toluenesulfonic acid is used as the extractant the best ratio of its amount to that of the picolines is 1:2.925.

The solubility of the organic solvent in water influences the effect of the separation. Results show that the value of separation factor is as high as 2.05 when n-heptane is used because of its lowest solubility.

The value of volume ratio of the mixtures, which is almost twice the original value by the single-stage dissociation extraction, is attractive, and this method of

separation has commendable potential for industrial exploitation compared with the results of single extractive distillation^[8].

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甲基吡啶的解离萃取分离实验研究

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摘要: 应用解离萃取分离合成吡啶产生的 3-甲基吡啶(3-MPD)与 4-甲基吡啶(4-MPD)的混合物(φ (3-MPD) = 68.472 2%; φ (4-MPD) = 26.517 6%), 对影响解离萃取分离的 6 个因素萃取剂、萃取剂的浓度及投料量、有机溶剂及投料量, 以及分离温度进行了研究. 选取了各因素的不同水平进行了六因素五水平的正交试验, 以有机相两甲基吡啶的体积比为主要考查对象, 筛选出了解离萃取分离甲基吡啶混合物的最佳工艺条件: 当甲基吡啶的混合物为 24 mL 时, 以浓度为 2 mol/L 的对甲基苯磺酸为萃取剂, 用量为 40 mL, 正庚烷为溶剂, 用量为 48 mL, 温度为 0 °C 时分离效果最好. 通过重复性实验, 分离效果得到明显提高, 说明此法具有工业化潜力.

关键词: 3-甲基吡啶; 4-甲基吡啶; 分离; 解离萃取; 正交试验

中图分类号: TQ028.8