

New process of preparation of pyrazolidine: synthesis, extraction and flow-sheet

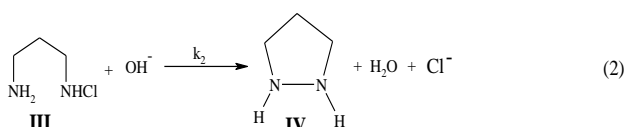
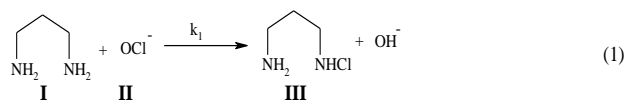
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1 Introduction

A new process for the preparation of the pyrazolidine (PYRZ), by intramolecular Raschig way has been developed in our laboratory [1, 2]. This work is divided into two parts: synthesis and extraction.

For the synthesis part: the reaction mechanism of the formation of pyrazolidine is carried out in two successive steps: the first involves the oxidation of 1,3-diaminopropane (**I**, DAP, $C_3H_{10}N_2$) by sodium hypochlorite (**II**, OCl^-) and formation of N, chloro-1,3-diaminopropane (**III**, $C_3H_9N_2Cl$). The second consists of a cyclization of N, chloro-1,3-diaminopropane (**III**) leading to pyrazolidine (**IV**).



This synthesis requires an excess of the diaminopropane (DAP) reagent, in comparison to sodium hypochlorite ($[DAP] / [OCl^-] = 8$), in order to increase the yield in pyrazolidine to 80%.

For the extraction process, these non-stoichiometric synthesis conditions imply then the (pyrazolidine / diaminopropane) separation and the recycling of the excess amine upstream of the synthesis. However, this is particularly difficult because of the very close physicochemical properties of these two compounds. In particular, the boiling temperatures of pyrazolidine (411 K, 1 bar) and 1,3-diaminopropane (409-410 K, 1 bar) differ by only 1 to 2 K, which leads to avoid implementing distillation operations.

The chosen extraction strategy requires a sequence of two stages:

- The first stage is a liquid-liquid phase separation, generated by the addition of solid sodium hydroxide.

The optimization of these extraction conditions requires knowledge of phase equilibria in the quaternary system H_2O -DAP-PYRZ- $NaOH$. The reaction solution is mainly composed of 27.2 %w in 1,3-diaminopropane, 3.7 %w in pyrazolidine, 5.7 %w $NaCl$, 0.1 %w $NaOH$ and 63.3 %w water, the amine will thus control the phenomenon of phase separation by solvent effect. We determined three isothermal sections (289 K, 313 K and 323 K) of the solid-liquid-liquid isobaric ternary system H_2O -DAP- $NaOH$ by ITA [3] (Isolethic Thermal Analysis) and acid-base titration.

- The second stage involves a selective precipitation of the two compounds in form of a salt by addition of hydrochloric acid. We determined and set three isothermal sections (283 K, 298 K and 333 K) of the isobaric solid-liquid ternary system H_2O -DAP.2HCl-PYRZ.2HCl by ITA. A final purification by selective crystallization is necessary in order to obtain high purity PYRZ.

2 Experimental

2.1 Apparatus

In order to determine the different ternary system H_2O -DAP- $NaOH$ and H_2O -DAP.2HCl-PYRZ.2HCl, several analytical methods were used: Isolethic Thermal analysis (ITA) was used to determine the limit tie-line and chemical analysis were used to determine the binodal curves.

2.2 Isolethic thermal analysis

This original method was developed in our laboratory [3]. It consists to follow the evolution of one or more physical properties of the system when its composition is modifying. For this study, liquid-solid equilibria were obtained by ITA, a device which permits to underline the transformations (crystallization, solubilization of a solid phase) of the system, in the course of addition of pure water for a constant reference temperature T_R . Thus, the

molar and mass compositions of the mixture evolve in a linear way during the analysis and determine so an isoplethic section in the ternary system.

The fluctuation of the temperature is obtained using the following equation:

$$\Delta T = (S \cdot \Delta H_D - \Delta H_d) \cdot V/K$$

Where:

S: solubility (g of substance/liter of solvent)

ΔH_D : weight enthalpy of dissolution ($J \cdot g^{-1}$ of substance)

ΔH_d : partial volumic enthalpy of dissolution ($J \cdot L^{-1}$ of substance)

V: rate of injection ($mL \cdot h^{-1}$)

K: cell constant ($W \cdot K^{-1}$)

Figure 1 represents a thermogram obtained by ITA for a mixture whose composition M is located in the invariant ternary triangle. It shows the evolution of the temperature during the addition of pure water to the mixture M.

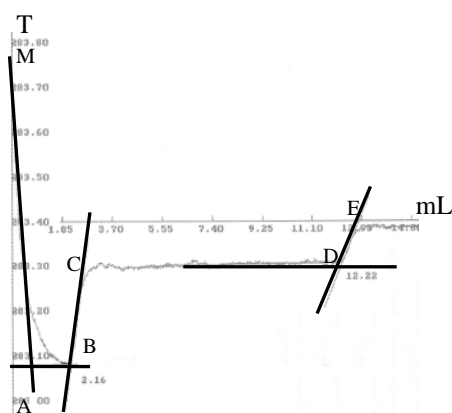


Figure 1. Thermogram obtained by ITA, $T = f(V_{H_2O})$.

Segment MA corresponds to the equilibrium of the triphasic system M. From A to B, the addition of pure water implies the dissolution of the $PYRZ \cdot 2HCl$ salt. At point B, the last crystals of dihydrochloride pyrazolidine disappear. Segment CD corresponds to the solid-liquid equilibrium between the saturated liquid and the $DAP \cdot 2HCl$ salt. At point D, the last crystals of dihydrochloride diaminopropane dissolve. Segment DE corresponds to the dilution of the system and the return to the equilibrium temperature. The B and D points correspond then to the end of dissolution of each salt. We denoted α , the solubility of the $DAP \cdot 2HCl$ in pure water and β , the solubility of $PYRZ \cdot 2HCl$ in pure water at 283K.

3 Results

3.1 Determination of the isobaric solid-liquid ternary system H_2O -DAP-NaOH

Three isothermal sections (293, 313 and 323 K) of the solid-liquid-liquid isobaric ternary system were determined.

Figure 2 show the isothermal sections obtained for the Water/Sodium Hydroxide/1,3-diaminopropane ternary system at 293 K.

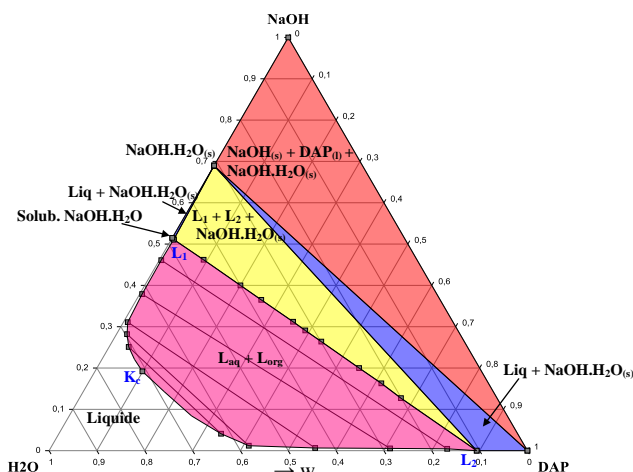


Figure 2. Solid-liquid-liquid isobaric ternary system H_2O -DAP-NaOH at $T = 293$ K.

All isotherms studied (293, 313 and 323 K) are characterized by 6 domains:

- a liquid monophasic domain in the water rich part
- one biphasic domain ($L_{aq} + L_{org}$)
- one triphasic three-phase triangle ($L_1 + L_2 + NaOH \cdot H_2O(s)$)
- two biphasic domains ($L + NaOH \cdot H_2O(s)$)
- one triphasic three-phase triangle ($NaOH(s) + NaOH \cdot H_2O(s) + Dap(l)$).

The evolution of liquid compositions of invariant mass versus temperature is presented in table 1.

Table 1. Massic compositions of the invariant liquid Li as function of the temperature.

T (K)	L_1 (aqueous phase)		L_2 (organic phase)	
	w (DAP)	w (NaOH)	w (DAP)	w (NaOH)
293	0.005	0.511	0.894	0
313	0.016	0.549	0.908	0.007
323	0.033	0.564	0.923	0.012

These results show the ineffectiveness of a temperature rise in the optimization of separation conditions by salting out with sodium hydroxide. The demixing temperature was set at 293 K. With this method, we can concentrate the hydrazine and the amine reagent, in particular at 293 K, we obtain an organic phase of: 15.4%w $PYRZ$, 71.7%w DAP and 12.9%w H_2O .

3.2 Determination of the isobaric ternary system solid-solid-liquid H_2O -DAP.2HCl-PYRZ.2HCl

Three isothermal sections (283, 293 and 333 K) of the solid-solid-liquid isobaric ternary system were determined. Figure 3. show the isothermal sections obtained for the H_2O -DAP.2HCl-PYRZ.2HCl ternary system at 293 K.

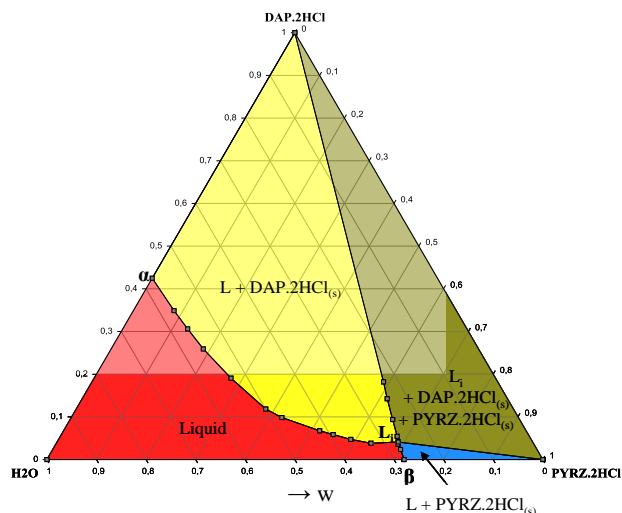


Figure 3. Solid-liquid ternary system H₂O-DAP.2HCl-PYRZ.2HCl at P= 1 bar and T = 333 K.

We denoted α , the solubility of the DAP.2HCl in pure water and β , the solubility of PYRZ.2HCl in pure water at 333K (the two binary diagrams Water-PYRZ.2HCl and Water-DAP.2HCl were determined by ATI, combined with DSC measurements).

All the isotherms studied are characterized by 4 domains:

- a liquid monophasic domain in the water rich part.
- one biphasic domain of crystallization of DAP.2HCl
- one biphasic domain of crystallization of PYRZ.2HCl
- one triphasic three-phase triangle ($L_i + \text{DAP.2HCl} + \text{PYRZ.2HCl}$).

For all the temperature range studied (283 to 333 K), the isotherms show a very large crystallization domain of the DAP.2HCl and a very narrow domain for the crystallization of PYRZ.2HCl, due to the high solubility of PYRZ.2HCl in water. This asymmetry leads to the elimination of the majority of DAP.2HCl by selective precipitation. The massic compositions of the invariant liquid, as function of the temperature, are presented in the table 2.

Table 2. Massic compositions of the invariant liquid L_i as function of the temperature.

T /K	% w PYRZ.2HCl	% w DAP.2HCl	% w H ₂ O
283	68,2	2,9	28,9
298	68,8	4,1	27,1
333	71	7,5	21,5

By this method, we can thus recycle a majority of the DAP reagent used in the synthesis, in particular, at 283 K, it is possible to recycle 97% of the diamino propane involved in the synthesis.

We obtain then an aqueous solution of pyrazolidine dihydrochloride titrating 68%w PYRZ.2HCl. A final purification by selective crystallization is necessary in order to obtain high purity PYRZ.

4 Conclusion

The synthesis process of pyrazolidine by the Raschig way is shown in figure 4.

- a) Reaction of diamino propane with sodium hypochloride in aqueous medium in order to form pyrazolidine ($p = [\text{DAP}]_0 / [\text{OCl}^-]_0 = 8$).
- b) Demixing of the reaction mixture obtained in step (a) by addition of anhydrous NaOH at T = 293 K and recovering of the organic phase.
- c) Precipitation of the DAP.2HCl salt by addition of hydrochloric acid at T = 283 K.
- d) Evaporation of excess water and filtration of the DAP.2HCl salt.
- e) Neutralization of the DAP.2HCl by addition of two equivalents of sodium hydroxide in order to obtain molecular diamino propane which is then recycled after distillation.
- e) Evaporation and filtration of the aqueous solution of pyrazolidine dihydrochloride.
- g) Final purification by selective crystallization in order to obtain high purity PYRZ.

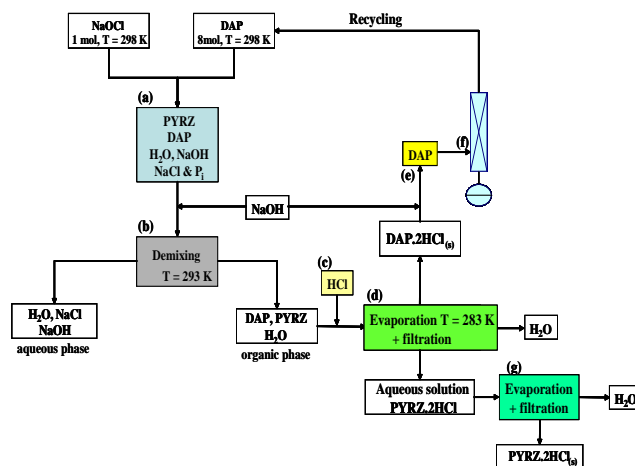


Figure 4. Process flow-sheet.

References

1. A. El Hajj, A.J. Bougrine, H. Delalu, Chemical Engineering Transactions **24** 31 (2011)
2. A. El Hajj, A.J. Bougrine, H. Delalu, Chemical Engineering Transactions **24** 1543 (2011)
3. J. Berthet, J.J. Counieux. Brevet F9313402, (1993)