Optimization of Adiponitrile Hydrolysis in Subcritical Water Using an Orthogonal Array Design

Peigao Duan · Yuanyuan Wang · Yan Yang · Liyi Dai

Abstract A study of the hydrolysis of adiponitrile (ADN) was performed in subcritical water to research the dependence on experimental conditions. An $L_{25}(5^6)$ orthogonal array design (OAD) with six factors at five levels using statistical analysis was employed to optimize the experimental conditions for each product in which the interactions between the variables were temporarily neglected. The six factors were adiponitrile concentration (ADN c, wt%), temperature (T), time (t h), percentage of additives (reactant/additive, wt/wt%), additives (A), and pressure (p, MPa). The effects of these parameters were investigated using the analysis of variance (ANOVA) to determine the relationship between experimental conditions and yield levels of different products. The results showed that (ADN c) and T had a significant influence on the yields of adipamide, adipamic acid, and adipic acid at $p < 0.05$. Time was the statistically significant factor for the yield of 5-cyanovalermic acid at $p < 0.05$ and (ADN c) was the significant factor for the yield of 5-cyanovaleramide at $p < 0.1$. Finally, five supplementary experiments were conducted under optimized conditions predicted by the Taguchi method; the results showed that the yield obtained of each product was no lower than that of the highest in the 25 experiments. Carbon balance was calculated to demonstrate the validity of the experimental technique and the reliability of the results. Based on the experimental results, a possible reaction mechanism was proposed.

Keywords Adiponitrile hydrolysis · Orthogonal array design · Subcritical water · Carbon balance · Mechanism

1 Introduction

Hydrolysis is a chemical reaction or process in which a chemical compound is broken down by reaction with water. Nitriles command special attention because of their appearance in industrial waste streams and in the product spectra from the reaction of aliphatic-

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NO$_2$-containing compounds in high-temperature water [1]. Most of the nitriles are industrially produced as intermediates and building blocks in organic synthesis and as organic solvents [2]. Therefore, it is very important to know how fast they hydrolyze because, in this way, waste streams can be cleaned. The hydrolysis of nitriles is also an area of great synthetic significance for the preparation of amides (e.g., acrylamide or nicotinamide) and carboxylic acids (e.g., R-(−)-mandelic acid and S-(+)-ibuprofen) in view of industrial applications and pharmacological interest in both classes of these compounds. At present, there is no completely satisfactory method for the conversion of nitriles to amides or acids. In practice, the reaction between nitriles and water would be so slow as to be completely negligible. Nitriles can be hydrolyzed under either acidic or alkaline conditions to make carboxylic acids or their salts [3, 4]. The final result is similar in both cases, but the exact nature of the final product varies depending on the conditions used for the reaction. Acid-catalyzed hydrolysis is used commercially for making amides from nitriles, and by further heating with water the amides can be hydrolyzed to acids with the production of ammonium salts [5]. Both the production of amides and acids, catalyzed by acid, can result in the formation of ammonium salts as by-products, which present a difficult handing and waste disposal problem. Increasing concern about water pollution can only mean an increasing and costly by-product disposal problem for the acid-catalyzed hydrolysis process. Hydrolysis of nitriles using alkali metal hydroxides was also reported in the literature [6, 7]. In this case, instead of getting an ammonium salt if the reaction only involved water, a sodium salt would be produced, which results in a sodium ion disposal problem and thus does not avoid the ecological problem [8]. Ammonia gas is given off as well. For example, sodium hydroxide can be used for the hydrolysis reaction, but again the sodium ion disposal problem exists. It is also known that ammonia at high temperature and for extended times will hydrolyze nitrile but this process also has problems. In the first place pressure equipment is required and in any long reaction time, yields suffer because by-products are frequently colored bodies which degrade product quality.

Water is an important material in the chemistry. It is generally agreed that water is an environmentally benign solvent, and its potential as a solvent depends on its unique system of hydrogen bonding. As water is heated, its normally strong hydrogen bonds are weakened, allowing dissociation that forms acidic hydronium ions and basic hydroxide ions [9, 10]. At the subcritical stage, the ion product, K_w, is up to three orders of magnitude larger than what it is at room temperatures and pressures. Subcritical water has properties similar to those of polar organic solvents such as ethyl alcohol or acetone. Its dielectric constant drops from 80 to 20, and its density drops from 1 to 0.7 g·cm^{-3}. Simply from the dissociation of water into acidic and basic ions, much larger amounts of acid and base are produced in subcritical water. We can use these acidic and basic ions to run acid-catalyzed and base-catalyzed reactions without the addition of mineral acids. Subcritical water also offers advantages in the most costly part of most chemical processes: separation of the chemical products [11, 12]. In subcritical processes, reaction products can be removed by cooling the water and reducing the pressure, dropping them out of the solution. Water-soluble catalysts can also be reused if they remain in the water. Use of subcritical water can also eliminate production of salts that result from the neutralization of acids used in conventional separations. Disposal of these salts can be a significant environmental issue.

Nitriles can hydrolyze in supercritical or subcritical water without the addition of any catalysts [13–15]. Thus far, many investigations have concentrated on the hydrolysis reactivity and kinetics of aliphatic and aromatic mononitriles, but few studies have been undertaken on dinitriles. We have successfully realized the hydrolysis of iminodiacetonitrile in subcritical water without the addition of any catalysts and the preparation of iminodiacetic acid salts assisted with additives [16, 17]. Adiponitrile (ADN) is the one of the important alkyl dinitriles,

which can hydrolyze partially or completely to produce valuable intermediates. Traditionally, the hydrolysis of ADN needs chemical catalysts which promote the hydrolysis reaction. Representative classes of catalysts primarily include nitrile hydratase, phosphoric acid or its salts, aliphatic or aromatic acid, etc. [18, 19]. The strong self-dissociation ability of subcritical water can offer rich sources of both hydronium cations and hydroxide anions, making it a potentially safe and environmentally compatible solvent, catalyst or reactant, in which hydrolysis reactions of ADN can be conducted. A statistical method was used to investigate the influence of the experimental parameters on the yield of different products.

Orthogonal array design (OAD), also known as the Taguchi method, is believed to incorporate the advantages of the simplex method and factorial design [20, 21]. It arranges different factors for effective optimization of the experimental conditions. The results of the OAD experiment can be statistically treated with two ways: analysis of variance (ANOVA) and direct observation analysis [22, 23]. In the ANOVA, the effects of different factors on response functions can be evaluated by both the significance (F ratio) and PC% (percentage contribution) values. In other words, the importance of a factor or the interaction among different factors can be estimated from the significance and PC% values. Direct observation analysis is also called range analysis, the fluctuation range and tendency of response functions versus the levels of different factors can be directly observed from a broken linear plot. Using ANOVA and direct observation analysis of the experimental results, factors that significantly affect the output responses can be found, and optimal parameters for an analytical procedure can be obtained. Use of OAD can also simplify the experimental procedures without affecting the quality of the results. Known as a chemometric method, OAD has been widely applied for the optimization of analytical procedures in recent years [23–25]. Here for the first time, we use OAD for the optimization of conditions for adiponitrile hydrolysis in the subcritical water system. In the present study, a $L_{25}(5^6)$ OAD procedure was performed with six factors (adiponitrile concentration, temperature, time, percentage of additives, additives, and pressure) at five levels since it was suitable for the conditions being investigated, and each experiment was repeated three times under the same conditions.

2 Experimental Sections

2.1 Materials

5-Cyanovaleramide (5-CVAM), 5-cyanovaleric acid (5-CVAC) and adipamic acid (ADAA) were prepared and purified according to methods reported in the literatures [26, 27]. Adipamide (ADAM) and adipic acid (ADA) were purchased from Aldrich. Adiponitrile was obtained from Alfa Aesar. Ammonia solution (25 wt-%), terephthalic acid and sodium sulfate were commercially available from China National Medicines Corporation Ltd. All the chemicals were used as received. Freshly double-distilled water was used throughout the experiments.

2.2 Procedures

Experiments were conducted in a 16.5 cm^3 316 stainless steel batch reactor consisting of a body and fastening cap. A common inlet and outlet was provided for charging and evacuating the reactor. The maximum possible working conditions of this reactor were 500 °C and 50 MPa. The temperature of the solution in the reactor was indirectly measured by a thermocouple inserting into a dip nozzle which was installed at about the middle of the

Fig. 1 Schematic representation
of batch reactor for subcritical
water generation
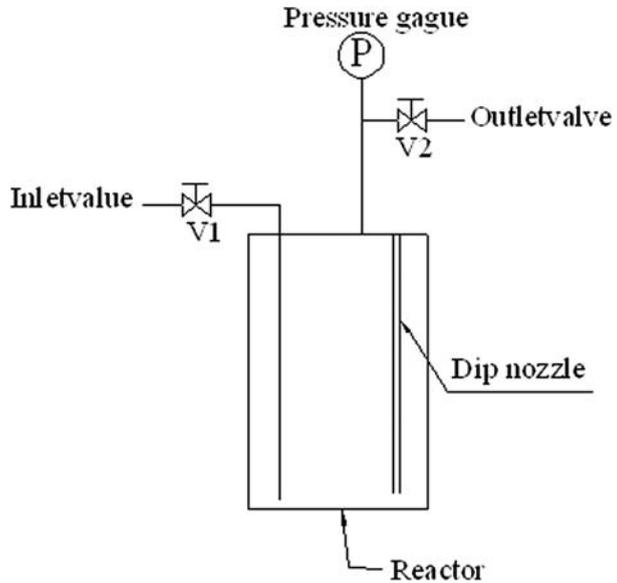
reactor (Fig. 1). The reactor was first loaded with reactant and double-distilled water and different amounts of additives before being sealed. The water loadings were selected such that 95% of the reactor volume would be occupied with liquid water at the reaction temperature. Water densities were taken from the steam tables [28]. The mass of reactant charged into the reactor was calculated based on $w_{\text{reactant}}/w_{\text{water}} \times 100\%$ at a given reactant concentration. The concentrations of reactant and additives in the solution were determined based on the solubility at room temperature. Prior to each experiment, the reactor was purged with high purity nitrogen for about 30 min to eliminate any air. The method of pressure control of the reaction system involved changing the amount of high purity nitrogen in the top of the reactor. Pressures given in the Table 2 are the total pressures which include the partial pressure of nitrogen and the water saturation vapor pressure at the desired temperature, ensuring that nearly a liquid phase was present throughout the reaction. It is preferable to insure, by adapting the pressure condition, that a liquid phase is present throughout the reaction. Under the experimental conditions, roughly no lower than 95% of the reactor volume was occupied by the liquid phase. In the case of the addition of aqueous ammonia, there was no change in the concentration of ammonia in the reaction solution after it was purged with high purity nitrogen as established by the titration with standard hydrochloric acid.

The loaded reactor was submerged in a pre-heated molten salt (components of sodium nitrate, potassium nitrate, sodium nitrite) tank preheated at 100 °C above the desired temperature. If the preheated temperature was set at the desired value, longer time would be required to reach the desired temperature. For example, at a given temperature of 250 °C, the salt bath was set at 350 °C and when the bath reached 350 °C, the loaded reactor was submerged directly into it. After about one minute, the temperature in the reactor reached 100 °C, then it increased rapidly for four minutes; the last minute was the transition to steady state. Five minutes later, the temperature reached 250 °C as described in Fig. 2. The temperature range of the process was determined by the hydrolysis degree of the ADN within the investigated range of time. At temperatures below 250 °C, the reaction rate was generally too low to be economically useful. At temperatures above 330 °C, significant amounts of by-products were formed. The reaction was carried out at a residence time of from two

Fig. 2 Temperature profile in the reactor and salt bath tank as a function of time (set temperature: 250 °C)
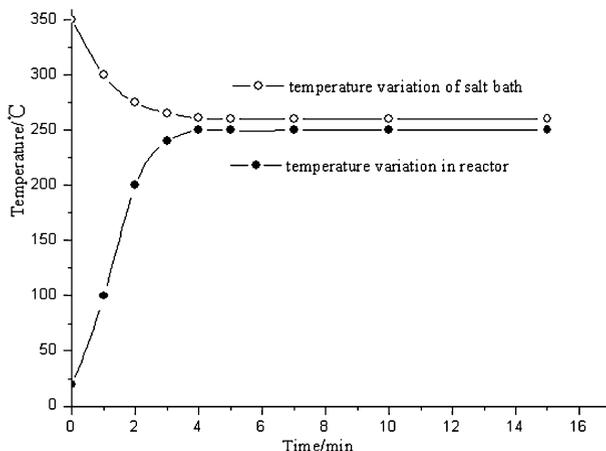
Fig. 3 Temperature profile in the reactor at quenching stage as a function of time (reaction temperature 250 °C)
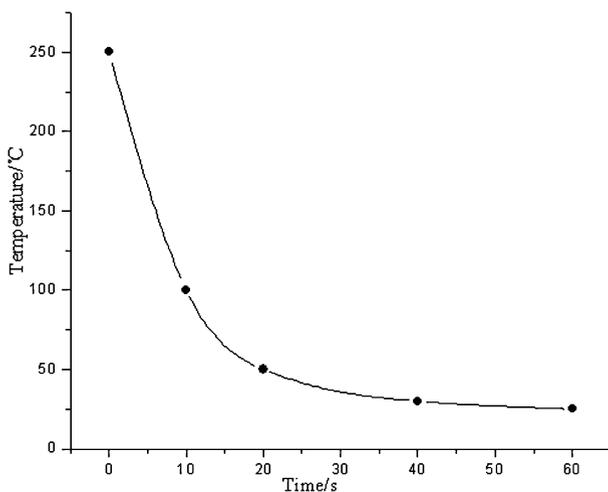
to six hours. A residence of below two hours generally gave too low a conversion, longer residence time also resulted in the formation of by-products. About five minutes later, the temperature in the reactor reached the desired temperature corresponding to zero reaction time. The temperature was controlled to maintain isothermal conditions within ±1 °C by an Omega temperature controller (precision of ±1 °C) assisting with a thermocouple inserting a dip nozzle into the reactor. At the end of each reaction, the reactor was removed from the molten salts tank and rapidly quenched in an ice bath water to stop the reaction. The temperature profile in the reactor at the quenching time is described in Fig. 3. One minute later, the temperature in the reactor reached the room temperature. The cooled system was first depressurized and the final reaction mixture was poured out of the reactor. Reactors were tested for leaks by weighing before and after each reaction. Hydrolysis products were recovered by rinsing the reactor with pure water three times and collected as the final resulting mixture.

The contribution of the preheating stage where the hydrolysis of ADN may proceed to some extent was subtracted by conducting blank experiments. The results of these blank

experiments revealed that lower-level conversion only occurred in the case of temperatures higher than 330 °C. While estimating the kinetic parameters, these conversions were duly accounted for. These experimental results were favorable for obtaining reaction kinetics information. The uncertainty in these estimated product yields reported herein was about 95% confidence interval for all of the products based on three replicate experiments.

The liquid samples obtained were quantitatively analyzed by a HPLC (Water 1525HPLC) equipped with an ODS C_{18} column (4.6 mm i.d., 250 mm, particle size 5 μm). The conditions used for the analysis were as follows: mobile phase of pH = 2.5, 25 mmol·dm^{-3} H_3PO_4 containing 1.1%v/v methanol in water; flow rate of 1.0 mL·min^{-1}; and a detection wavelength of 200 nm. Product identification was achieved by comparing the results with those for a standard solution of pure compounds and inspecting the high-performance liquid chromatography-mass spectra.

2.3 Orthogonal Array Design

To seek optimal conditions for the yield of each product, the effects of some parameters on the hydrolysis of ADN were investigated. A $L_{25}(5^6)$ OAD was used in the present hydrolysis procedure to optimize the experimental conditions for obtaining a high yield of different products. It was noteworthy that appropriate selection of the factors of OAD could simplify the experimental procedures without affecting the quality of results. The design involved six factors at five levels as shown in Table 1. The order of experiment was obtained by inserting parameters into columns of an orthogonal array and the experimental order was made random and is presented in Table 2. The interactive effect of the parameters was not taken into consideration because some preliminary tests showed that they could be neglected. Each of the 25 experiments was performed in triplicate, corresponding to a total of 75 tests. For the additives factor, we chose different kinds of additives (including no additive) to investigate their effects on the hydrolysis rate of ADN and the distribution of the reaction products. We observed the pH effect with the addition of ADA, terephthalic acid (PTA), $NH_3·H_2O$ and the neutral salt of Na_2SO_4. The analysis of data when there is no interaction includes (1) determining the optimal conditions, (2) identifying the individual influence of each factor, and (3) estimating the performance of the hydrolysis of ADN at the optimal conditions.

Table 1 Experimental parameters and their levels in $L_{25}(5^6)$ OAD

Parameters	Levels				
	1	2	3	4	5
ADN concentration (wt-%)	1	2	4	6	8
Temperature (°C)	250	270	290	310	330
Time (h)	2	3	4	5	6
Percentage of additives[a]	2	4	6	8	10
Additives	No[b]	ADA	PTA	$NH_3·H_2O$	Na_2SO_4
Pressure (MPa)	14	20	27	35	43

[a]Ratio of additive/ADN (wt/wt)

[b]Without additives

**Table 2** $L_{25}(5^6)$ OAD matrix randomize experimental plan table

No.	ADN con. (wt-%)	T (°C)	t (h)	A/R (wt/wt)%	Additive	p[a] (MPa)
1	1	250	2	2	None	14
2	1	270	3	4	ADA	20
3	1	290	4	6	PTA	27
4	1	310	5	8	$NH_3 \cdot H_2O$	35
5	1	330	6	10	Na_2SO_4	43
6	2	250	3	6	$NH_3 \cdot H_2O$	43
7	2	270	4	8	Na_2SO_4	14
8	2	290	5	10	None	20
9	2	310	6	2	ADA	27
10	2	330	2	4	PTA	35
11	4	250	4	10	ADA	35
12	4	270	5	2	PTA	43
13	4	290	6	4	$NH_3 \cdot H_2O$	14
14	4	310	2	6	Na_2SO_4	20
15	4	330	3	8	None	27
16	6	250	5	4	Na_2SO_4	27
17	6	270	6	6	None	35
18	6	290	2	8	ADA	43
19	6	310	3	10	PTA	14
20	6	330	4	2	$NH_3 \cdot H_2O$	20
21	8	250	6	8	PTA	20
22	8	270	2	10	$NH_3 \cdot H_2O$	27
23	8	290	3	2	Na_2SO_4	35
24	8	310	4	4	None	43
25	8	330	5	6	ADA	14

[a]Pressure was the total pressure of the partial pressure of nitrogen and the water saturation vapor pressure at desired temperature

3 Results and Discussions

3.1 Identification of Intermediate Compounds and Final Products

There were five compounds resulting from the hydrolysis of ADN, including 5-cyanovaleramide, adipamide, 5-cyanovaleric acid, adipamic acid, and adipic acid detected by HPLC (Fig. 4). Table 3 shows the analysis of hydrolysis products at different experimental conditions. Under the conditions of higher temperatures and pressures, 5-cyanovaleramide resulting from the first step of ADN hydrolysis would preferably be converted to adipamide than to 5-cyanovaleric acid, so some 5-cyanovaleric acid remained in the products along with the proceeding of the reaction.
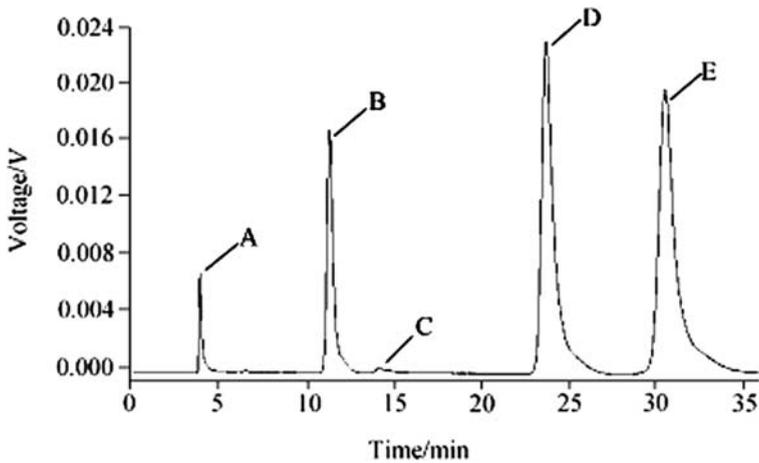
Fig. 4 Chromatograph of the different hydrolysis products of adiponitrile in subcritical water assisted with 6% $NH_3 \cdot H_2O$ at a temperature of 250 °C, time of 3 h, pressure of 30 MPa. *A* adipic acid, *B* adipamide, *C* 5-cyanovaleric acid, *D* 5-cyanovaleramide, *E* adipamic acid

Table 3 Hydrolysis product analysis

No.	ADAM	ADAA	5-CVAM	5-CVAC	ADA
1	1.20[b]	1.67	14.99	ND[c]	ND
2	1.63	11.67	15.84	ND	0.30
3	1.17	16.45	1.21	0.06	4.92
4	2.94	16.30	13.73	0.11	1.30
5	0.10	2.61	0.20	0.54	ND
6	0.01	ND	0.09	ND	ND
7	2.33	23.43	2.17	ND	1.40
8	2.44	20.99	0.75	0.30	4.30
9	2.91	25.12	1.09	0.72	2.80
10	0.99	8.93	0.59	ND	22.07
11	1.75	11.20	13.02	0.17	17.74
12	5.01	25.76	1.67	0.40	17.20
13	3.31	17.96	0.11	0.32	2.07
14	3.62	20.64	4.33	0.01	3.13
15	1.14	7.35	0.30	0.50	15.63
16	6.30	32.77	5.29	0.02	1.80
17	7.82	35.82	0.15	0.58	4.45
18	9.60	42.48	3.36	ND	2.31
19	7.18	28.08	1.16	0.02	2.86
20	1.50	4.69	3.47	0.40	13.89
21	7.20	24.81	7.18	0.22	2.58
22	12.13	28.18	7.29	0.08	2.09
23	13.00	31.92	0.24	ND	1.47
24	6.36	13.56	0.27	0.30	7.90
25	0.76	1.86	0.28	0.80	6.78

[a]The uncertainty in these estimated products yield reported herein is about 95% confidence interval for all of the products

[b]Percentage of weight (wt-%)

[c]"ND" signifies that the material was not detected

Fig. 5 Carbon balance for the ADN hydrolysis in high-temperature water
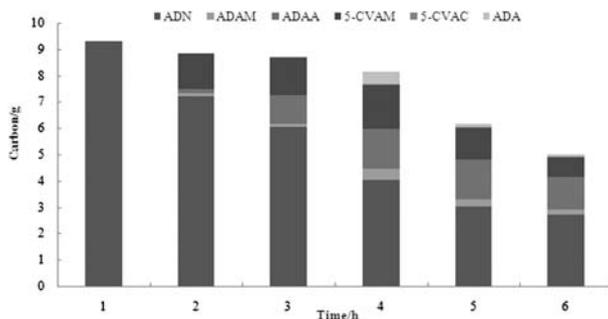
Table 4 Carbon balance for the hydrolysis of ADN at high temperature water

t (h)	ADN	ADAM	ADAA	5-CVAM	5-CVAC	ADA
0	9.30×10^{-2}	0	0	0	0	0
2	7.21×10^{-2}	1.10×10^{-3}	0.15×10^{-2}	1.37×10^{-2}	0	0
3	6.03×10^{-2}	1.49×10^{-3}	1.07×10^{-2}	1.45×10^{-2}	0	0.28×10^{-3}
4	4.05×10^{-2}	3.92×10^{-3}	1.51×10^{-2}	1.72×10^{-2}	0.06×10^{-3}	4.48×10^{-3}
5	3.03×10^{-2}	2.69×10^{-3}	1.49×10^{-2}	1.26×10^{-2}	0.10×10^{-3}	1.19×10^{-3}
6	2.73×10^{-2}	1.93×10^{-3}	1.24×10^{-2}	0.71×10^{-2}	0.50×10^{-3}	0.81×10^{-3}

3.2 Carbon Balance

The carbon balance of the hydrolysis process was calculated to demonstrate the effectiveness of the experimental technique and the reliability of the results. The total carbon charged into the reactor was the content of carbon in adiponitrile. The total carbon in the hydrolysis reaction mixture is the sum of the masses of carbon in adiponitrile, 5-cyanovaleramide, 5-cyanovaleric acid, adipamide, adipamic acid and adipic acid. The carbon mass was calculated based on the content of these compounds in the reaction mixture detected by high performance liquid chromatography. Changes of the overall carbon weight in the reaction mixture between particular stages can be observed in Fig. 5. The content of carbon in each product is also listed in Table 4. The specification of the process enables the process to be monitored and provides an easy comparison of the participation of the main substances in the whole hydrolysis scheme. The same type of carbon balance was calculated for all experiments. If the amounts of carbon in the reactant and the reaction mixture were computed, the ratio of carbon charged into the reactor to the carbon in the final reaction mixture can be determined as C% mass balance = (Output C ÷ Input C) × 100%. Due to possible side reactions, especially at high temperatures and longer reaction times, the average deviation of the carbon balance was 46% as presented in Fig. 5.

3.3 ANOVA analysis of the OAD

The purpose of the OAD was to select the optimal experimental parameters for obtaining a maximum yield of each product that would form adipamide rather than convert to 5-cyanovaleric acid, resulting in little of the latter remaining in the products. Statistical analysis of variance (ANOVA) was performed to see whether the process parameters were statistically significant. The significance (F ratio) analysis is shown in Table 5 where the

Table 5 ANOVA analysis and percent contribution for the yield of each products in the $L_{25}(5^6)$ OAD matrix

Source of variation	SS[a]	Degree of freedom	Mean square	F[b]	SS'[c]	$PC\%$[d]
5-CVAM						
ADN c (wt-%)	194.9	4	48.7	4.40[**]	170.6	27.0
T (°C)	181.8	4	45.5	4.09	157.5	25.3
t (h)	49.4	4	12.4	1.00	25.1	3.8
A/R (wt/wt)%	50.4	4	12.6	1.29	26.1	3.8
A	69.3	4	17.3	1.65	45.0	6.8
p (MPa)	95.3	4	23.8	1.98	70.9	10.7
Error	24.3	4	12.4	–	150.6	22.6
Total	665.3	28	–	–	665.3	100.0
ADAM						
ADN c (wt-%)	170.7	4	42.7	20.24[*]	162.3	49.4
T (°C)	86.2	4	21.6	10.22[*]	77.8	23.7
t (h)	24.0	4	6.0	2.85	15.6	4.8
A/R (wt/wt)%	16.2	4	4.0	1.92	7.8	2.4
A	8.4	4	2.1	1.00	0.0	–
p (MPa)	14.4	4	3.6	1.71	6.0	1.8
Error	8.4	4	2.1	–	50.4	12.9
Total	328.3	28	–	–	328.3	100.0
ADAA						
ADN c (wt-%)	983.4	4	245.9	8.34[*]	865.5	26.8
T (°C)	1508.7	4	377.2	12.80[*]	1390.8	46.7
t (h)	202.5	4	50.6	1.72	84.6	2.6
A/R (wt/wt)%	170.5	4	42.6	1.45	50.0	1.5
A	249.5	4	62.4	2.12	131.6	4.2
p (MPa)	117.9	4	29.5	1.00	0.0	–
Error	117.9	4	29.5	–	589.5	18.2
Total	3232.5	28	–	–	3232.5	100.0
5-CVAC						
ADN c (wt-%)	0.07	4	0.02	1.00	0.04	2.6
T (°C)	0.39	4	0.10	5.67	0.36	22.7
t (h)	0.66	4	0.17	9.58[*]	0.63	40.9
A/R (wt/wt)%	0.12	4	0.03	1.70	0.09	5.8
A	0.23	4	0.06	3.36	0.20	13.8
p (MPa)	0.08	4	0.02	1.19	0.05	3.5
Error	0.03	4	0.02	–	0.18	11.0
Total	1.59	28	–	–	1.59	100.0
ADA						
ADN c (wt-%)	207.6	4	51.9	7.64[*]	192.4	21.2
T (°C)	254.8	4	63.7	9.37[*]	239.6	26.6
t (h)	127.1	4	31.8	4.68	111.9	11.7
A/R (wt/wt)%	27.2	4	6.8	1.00	12.0	1.3
A	154.8	4	38.7	5.69	139.6	14.6
p (MPa)	167.6	4	41.9	6.16	152.4	16.0
Error	15.2	4	3.8	–	91.2	9.6
Total	954.4	28	–	–	954.4	100.0

[a] Sum of square

[b] $F_{\text{critical}} = 6.39$ ([*] $p < 0.05$), 4.11 ([**] $p < 0.1$)

[c] Sum of square-sum of square of error

[d] Percentage contribution $= (SS'/SS_{\text{total}}) \times 100$

[**], [*] Significant factor

critical F value for each process parameter indicates which parameter has the most significant influence on the yield of different hydrolysis products. For example, if one of the F values is larger than those of any others, it has the greatest effect on the yield of the given product due to the change of the process parameters. It can be seen that (ADN c) and T have significant influences on the yields of adipamide, adipamic acid and adipic acid at $p < 0.05$, where each p value represents twice the probability that the true value has any value with a sign opposite to that of the observed value; t was the statistically significant factor on the yield of 5-cyanovalermic acid at $p < 0.05$; (ADN c) was the significant factor on the yield of 5-cyanovaleramide at $p < 0.1$. The F value for all factors is bigger than the extracted F value from the table. This means that the variance of all factors is significant compared with the variance of error, which indicates the variance of error has no meaningful effect on the response. These analysis of variance results are further confirmed by the analysis of percentage ($PC\%$) contribution contained in Table 5. The $PC\%$ is obtained by the equation as follows:

$$PC\% = SS'/SS_{\text{total}} \times 100\%; \qquad \text{Mean square} = SS/\text{degree of freedom}$$

where SS' signifies the sum of squares and is calculated by $(SS - SS_{\text{error}})$, SS is the individual sum of squares, SS_{error} is the sum of squares of error, and SS_{total} is the total sum of squares of all factors. Obviously, the value of SS'_{total} is equal to SS_{total} in statistics, whereas SS'_{error} is obtained from the difference of SS_{total} and the sum of SS' of the considered factors. The results imply that (ADN c) is the most important factor contributing to the yield of 5-cyanovaleramide (27.0%) and adipamic acid (49.4%); T is the most significant factor contributing to the yield of adipamide (46.7%) and adipic acid (26.6%); the t percentage contribution is the biggest to the yield of 5-cyanovaleric acid (40.9%).

Apparently the data analysis of $PC\%$ is in good agreement with the conclusion obtained from the significance analysis discussed above. Three factors, including (ADN c), T and t had remarkable influences on the hydrolysis reaction products distribution. Control of the hydrolysis product distribution can be realized based on the significance of each factor on different product yields.

3.4 Direct Observation Analysis of the OAD

The impact of parameters on the yield of each product can also be statistically treated with direct observation analysis to evaluate the effect or the importance of a given factor. In the direct observation analysis of the OAD, the average yield (k) of each product at each level of a factor is obtained from the data listed in Table 3, and the results are listed in Table 6. The mean value of each product yield for the corresponding factors and at each level was calculated according to the assignment of the experiment. For example, the performance statistics of the first value of k_1 (9.19) for the 5-CVAM is thus the average of those obtained from the experiment with experiment numbers of 1, 2, 3, 4 and 5. Experimental conditions for the first value of k_2 (0.94) for 5-CVAM are the conditions of the experiment with numbers of 6, 7, 8, 9 and 10, and so on. The mean values of the five levels of each factor (e.g., temperature) reveal how the product yields will change when changing the levels of that factor. In all cases, it should be noted that each reported product yield was the average of five measurements, for each of which the parameter of interest was keep constant, and the other parameters were changed (Table 2). It is impossible that the effects of the other variables, which are not constant in the data used to calculate an average k, are likely to convolute the interpretation of the effect of the examined variables. The optimal conditions

Table 6 The average products yield (k) at each level of a factor and ranges

	ADN c (wt/wt)%	T (°C)	t (h)	A/R (wt/wt)%	Additive	p (MPa)
5-CVAM						
k_1	9.19	8.11	6.11	4.29	3.29	3.74
k_2	0.94	5.24	3.53	4.42	6.72	7.03
k_3	3.89	1.13	4.03	1.21	2.36	3.11
k_4	2.69	4.11	4.34	5.35	4.94	5.55
k_5	3.05	0.97	1.75	4.48	2.45	1.12
Range	8.26	7.15	4.37	4.14	4.36	5.91
ADAM						
k_1	1.42	3.29	5.51	4.27	3.79	2.96
k_2	1.74	5.78	4.59	3.72	3.33	3.73
k_3	2.97	5.90	2.62	2.68	4.31	4.19
k_4	6.48	4.60	3.49	4.64	3.98	5.30
k_5	7.89	0.90	4.27	4.72	5.07	4.22
Range	6.48	5.06	2.89	2.05	1.74	2.34
ADAA						
k_1	9.65	14.09	20.38	17.71	15.88	14.60
k_2	15.69	24.97	15.68	16.89	18.47	19.53
k_3	16.58	25.83	13.87	14.95	20.81	9.09
k_4	28.77	20.74	19.54	22.87	13.43	20.71
k_5	19.94	5.00	22.87	18.12	22.06	16.79
Range	19.12	20.84	7.31	7.92	8.63	6.11
5-CVAC						
k_1	0.06	0.14	0.02	0.77	0.30	1.21
k_2	0.02	0.65	0.24	0.41	0.88	0.15
k_3	1.28	0.39	0.22	0.84	0.73	0.33
k_4	0.14	0.04	1.49	0.34	0.53	0.04
k_5	1.00	1.28	0.53	0.14	0.06	0.73
Range	1.26	1.24	1.47	0.70	0.82	1.17
ADA						
k_1	1.30	4.42	6.15	6.07	6.46	2.62
k_2	6.34	4.09	4.05	7.05	5.99	2.58
k_3	10.25	3.01	9.17	3.86	9.15	6.86
k_4	5.06	3.60	5.28	4.64	3.87	9.63
k_5	4.16	11.88	2.38	5.40	1.56	4.48
Range	8.85	8.87	6.79	3.20	7.59	7.06

for the yield of each product are presented in Table 7. The determination of the optimal conditions for each product is based on the maximum k value of that particular parameter given in Table 6. According to these findings and the significant effects by the OAD method, results for the combination of levels could be predicted, and the predications are confirmed

Table 7 The optimal conditions for the yields of each product

Optimal parameters	ADN c wt-%	T (°C)	t (h)	A/R (wt/wt)	Additive	p (MPa)
5-CVAM	1%	250	2	8%	ADA	25
ADAM	8%	290	2	8%	Na_2SO_4	25
ADAA	6%	290	6	8%	Na_2SO_4	25
5-CVAC	4%	330	5	6%	ADA	10
ADA	4%	250	4	4%	PTA	25

Table 8 Experimental and optimized yield of each product

	Yield wt-%				
	ADAM	ADAA	5-CVAM	5-CVAA	ADA
Experimental[a]	13.00	42.48	15.84	0.80	22.07
Optimized[b]	13.56	43.05	15.90	0.80	22.49

[a]The highest yield in the experiment

[b]Optimized conditions by the Taguchi method

by some experiments. The results from the confirmatory experiments showed that under the optimal conditions, obtained from the ANOVA analysis, the yield of each product is no lower than that of the maximum point in each graph, which are presented in Table 8. Optimal combination of the process parameters can be predicted using ANOVA analysis and the performance characteristics.

From the direct observation analysis of the results in Table 6, some data are scattered or deviate unexpectedly, but it allowed us to identify conditions that optimize each of the products. This work and approach would be useful to other high-temperature water systems for optimizing product yields. The significance of each parameter on the hydrolysis products is primarily based on the ANOVA, direct observation analysis is just an additional way to validate the ANOVA results.

3.5 Effect of ADN Concentration on Product Yield

The effect of reactant concentration on the yield of each product was investigated with varying amounts of ADN in water as shown in Table 6. As can be seen, when the concentration of ADN increases, the yield of 5-CVAM decreases, and the yield of ADAM, ADAA and ADA increase up to a maximum followed by a decrease. There was a strong effect of the reactant concentration on the yields of 5-CVAM, ADAM and ADAA. At lower reactant concentrations, the hydrolysis product was primarily 5-CVAM, but at higher reactant concentrations, ADAM, ADAA and ADA were the major products. There is no obvious effect of the change of the reactant concentration on the yield of 5-CVAC. A possible explanation for this result is that at lower reactant concentration, the formation rate of the 5-CVAM is faster than its hydrolysis rate, which means that hydrolysis of 5-CVAM is the rate-determining step. With increasing reactant content in the water, the accumulation of products resulting from the first hydrolysis step also increases, and the hydrolysis rate of 5-CVAM increases, resulting in a higher yield of the secondary products, suggesting autocatalytic kinetics for this reaction system.

3.6 Effect of Temperature on Product Yield

Variation of temperature affects the properties of the water and the interaction among additive, reactant and water molecules as well as the distribution of the products, accordingly. Lower temperature is advantageous for the formation of 5-CVAM. At a temperature of about 275 °C, high yields of ADAM and ADAA were obtained. If the temperature increased gradually, ADAM and ADAA would convert to ADA. At higher temperature, ADA was the main product and also the final reaction product, consistent with the results of the ANOVA analysis. Generally, higher temperature favors the yield of adipic acid. Increasing the temperature leads to contrary effects for the production of adipic acid. The ion product decreases with increasing temperature at ranges from 250 to 330 °C, resulting in a lower concentration of H^+, but higher pH is disadvantageous for the yield of ADA as discussed in the section "Effect of the Kind of Additives on Product Yield". On the other hand, increasing temperature can accelerate the reaction rate, since the hydrolysis reaction is an endothermal reaction and the equilibrium will shift in a positive direction following Le Chatelier's Principle, resulting in the increase of ADA yield. The fact that the yield shows a somewhat decreasing trend to 290 °C under these experimental conditions is a negative effect because of the decrease of the ion product with increasing temperature exceeds the enhancement effect. The combined result is a decrease in the yield of ADA, because of increasing temperature in the range 250–290 °C. At higher temperatures ranging from 290 to 330 °C, the negative effect on the ion product is less than the enhancement effect of increasing the temperature; the combined result is an increase of ADA yield.

3.7 Effect of Time on Product Yield

The effect of time on the yield of different products was realized by conducting the hydrolysis of ADN at different reaction time intervals. The variation range of k of each product with the change of time is listed in Table 6. There was no remarkable influence of time on the yield of 5-CVAM, ADAM, ADAA and ADA except for 5-CVAC. More specifically, the yield of 5-CVAM on the whole was decreased, suggesting that 5-CVAM did not exist for long in subcritical water. There was a similar variation trend of the yield of ADAM and ADAA, both in lower yields at the same reaction time of four hours. Although the yield of 5-CVAC mainly depended on reaction time, the maximum value was only 1.49 wt-%, so the preparation of 5-CVAC was not accomplished with the adjustment of time. Longer reaction time was unfavorable for the accumulation of ADA possibly because of its thermal decomposition.

3.8 Effect of A/R Ratio on Product Yield

As can be seen in Table 6, a change of the additive content in the reaction system had no obvious influence on the yield of each product, that is to say whether the additives existed or not, hydrolysis of ADN could take place freely. Experiments on the hydrolysis of ADN in subcritical water without the addition of any additives in entries 1, 8, 15, 17 and 24 proved this result.

3.9 Effect of the Kind of Additives on Product Yield

Introduction of the additives into the reaction system could change the pH or the ionic strength. In the presence of acid or base, the pH in the reaction solution would be changed.

Increase of the concentration of H$^+$ or OH$^-$ in the reaction system could accelerate the hydrolysis of ADN. The investigated results showed that the existence of acidic or basic additives could only promote the hydrolysis rate of ADN, resulting in a shorter reaction time from the beginning of the reaction to the end. Additives have no significant influence on the yields of all products just as described in Table 6. There is a little increase of the yield of ADAM with the addition of Na$_2$SO$_4$, possibly because water molecules solvating the ionic species of the dissolved salt and the local density of the surrounding water is expected to increase. Increase of the water density around the salt species results in an increase of the dielectric constant of this region, which causes an increase of the hydrolysis reaction rate of ADN. PTA was the most effective additive for the production of ADA, whereas basic or neutral salts were the least effective additive. ADA was the optimal additive for the preparation of 5-CVAC, suggesting that low pH was suitable for the presence of 5-CVAC in high-temperature conditions. There is no trend to follow for effects of the additives on the yield of 5-CVAM.

### 3.10 Effect of Pressure on Product Yield

Generally, the variation of pressure on the reaction system leads to an increase of the water density, directly resulting in an increase of the H$^+$ concentration; on the other hand, increasing the water density can promote the dissociation of PTA, also increasing the H$^+$ concentration. Pressure plays an important role in the production of ADA, but not as well as for the other products presented in Table 6. An increase in pressure causes an increase in the fluid density and thus it has a double effect: an increase of the concentration of H$^+$ results in an increase in the yield of ADA; higher pressure is unfavorable for the hydrolysis reaction according to Le Chatelier's Principle. If the enhancement effect of increasing the H$^+$ concentration due to increasing pressure is less than the negative effect of reacting in such a way as to produce fewer molecules due to the increase of pressure, the position of equilibrium will move in the direction so that the pressure is reduced again. The combined result is the decrease of ADA yield.

3.11 By-products in the Reaction at above 330 °C

Formation of by-products was suggested under the conditions of longer reaction time and higher temperature as shown in the carbon balance analysis and the discussion section of effect of temperature on product yield. Under the conditions of longer reaction time and higher temperature, the final hydrolysis reaction product was primarily ADA which is a dicarboxylic acid. It can be produced by the consecutive oxidation to lower molecular weight dicarboxylic acids [29]. The oxidation of dicarboxylic acids was also accompanied by oxidative decarboxylation, leading to the formation of monocarboxylic acids. Total yields of five products reached 11% as shown in Table 3 for run No. 25. The low yield value suggested the presence of other by-products, and the carbon balance analysis at different temperatures also gave a proof of this result.

4 Analysis of the Reaction Mechanism

In the first hydrolysis step of ADN, there is no competitive reaction pathway, and it only involves the transformation of the cyano group to the amide group. If the two cyano groups in adiponitrile were attacked simultaneously, no 5-cyanovaleramide would be formed. Actually, the higher content of 5-cyanovaleramide was detected at lower temperatures and shorter
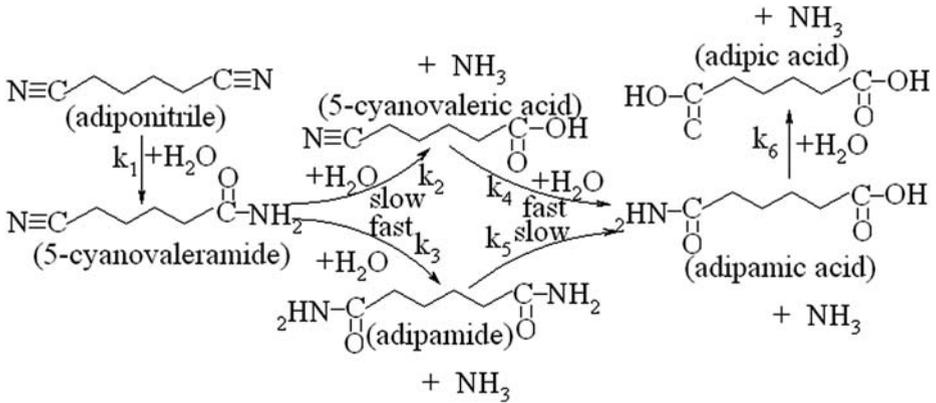
Fig. 6 Global reaction scheme for the hydrolysis of ADN in NCW

reaction times, suggesting that the two cyano groups transform to amides in sequence. There could be two possible reaction pathways for the hydrolysis of 5-cyanovaleramide: first if the cyano group or the amide group was attacked initially and second if the cyano group was attacked first, adipamide was primarily formed and detected with higher content in the products; on the contrary, if the amide group was firstly attacked, 5-cyanovaleric acid was primarily formed and detected with higher content in the products. The experimental re- sult was that the content of adipamide was much higher than that of 5-cyanovaleric acid in the products, suggesting hydrolysis of 5-cyanovaleramide proceeded basically by the trans- formation of the cyano group to the amide group. Hydrolysis of adipamide is similar to that of adiponitrile in that only one of the amides was attacked to form the adipamic acid which could further be hydrolyzed to form adipic acid. Based on the hydrolysis steps men- tioned above, a hydrolysis mechanism of adiponitrile can be proposed as described in Fig. 6. The concentration of ADN is the significant factor on the yield of 5-cyanovalericamide, the lower content of ADN in the solution, and the higher yield of 5-CVAM. There are two steps to follow for 5-cyanovalericamide, $step_2$ and $step_3$. The concentration of ADN and temper- ature are the significant factors on the yield of adipamide. Higher concentrations of ADN and moderate temperature are the preferable conditions for a higher yield of adipamide. Reaction time is a considerable factor for the formation of 5-cyanovaleric acid. Under the conditions of moderate concentration and temperature, 5-cyanovaleric acid and adipamide can convert to adipamic acid, which is more stable than 5-cyanovaleric acid in the investi- gated conditions. The formation rate of 5-cyanovaleric acid is slower than of its hydrolysis rate, resulting in lower concentrations of 5-cyanovaleric acid in the final products. As sug- gested by the results in Table 6, higher temperature is advantageous for the reaction $step_6$, indicating the relative stability of adipic acid at higher temperature.

5 Conclusions

In this study, an orthogonal array design (OAD) was employed to optimize the experimental conditions of adiponitrile hydrolysis in subcritical water. Influences of six factors on the yields of different products were considered. Results of the OAD experiments were treated statistically by ANOVA and direct observation analysis. The results showed that (ADN c) and T had significant influence on the yields of adipamide, adipamic acid and adipic acid

at $p < 0.05$; T was the statistically significant factor for the yield of 5-cyanovalermic acid at $p < 0.05$, and (ADN c) was the significant factor for the yield of 5-cyanovaleramide at $p < 0.1$. The carbon balance was calculated. Based on the results for each product detected and its yield under different conditions, a possible reaction mechanism was proposed.

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