

Pei-Gao Duan<sup>1,2</sup>  
Shuang Li<sup>1</sup>  
Yan Yang<sup>1</sup>  
Zhi-Zhong Wang<sup>1</sup>  
Li-Yi Dai<sup>1</sup>

Research Article

## Green Medium for the Hydrolysis of 5-Cyanovaleramide

<sup>1</sup> Shanghai Key Laboratory of Green Chemistry and Green Process, Department of Chemistry, East China Normal University, Shanghai, P.R. China.

<sup>2</sup> Department of Chemical Engineering, The University of Michigan, Ann Arbor, USA.

Hydrolysis of 5-cyanovaleramide (5-CVAM) in near-critical water without the addition of any catalyst has been demonstrated. The results demonstrated that the cyano group at one end of the carbon of 5-CVAM is more reactive than the amide group at the other end, under the same experimental conditions. The relations between 5-CVAM concentration and residence time revealed that hydrolysis of 5-CVAM shows second-order reaction kinetics in the investigated temperature range. The rate constants, average apparent activation energy and pre-exponential factor were evaluated according to the Arrhenius equation. Based on the experimental results, a carbon balance was calculated, and a hydrolysis reaction scheme of 5-CVAM was proposed.

**Keywords:** 5-Cyanovaleramide, Green solvent, Hydrolysis, Kinetics, Near-critical water

*Received:* November 18, 2008; *revised:* December 13, 2008; *accepted:* December 17, 2008

**DOI:** 10.1002/ceat.200800607

### 1 Introduction

Water near its critical region, namely near-critical water (NCW), has the capability of dissolving a variety of organic solutes, since its dielectric constant can be adjusted as a function of temperature under external pressure [1–5]. It is also a compressible fluid; however, the compressibility is very small, so very large pressures are required to get any appreciable compression of the fluid. In addition, most of its properties are different in its physical and chemical features, e.g., below the critical temperature and at high pressures the ionic product is up to three orders of magnitude higher than under ambient conditions. Up to now, many specific synthesis reactions have been conducted using water in its near-critical or supercritical region without the addition of any catalyst [6–10]. In all synthesis reactions, water can participate in reactions as an acid/base catalyst or catalyst precursor that modifies and stabilizes the transition state, and it can also be the reactant or product of the synthesis reactions.

Recently, NCW has been demonstrated to be a viable medium for conducting hydrolysis reactions on a variety of organic compounds [11–15]. At present, these organic compounds primarily include amines/imines, amides, nitriles, nitro compounds, esters, ethers, acetals, alkyl halides, anhydrides, and silanes [4]. Nitriles command special attention because of their appearance in industrial waste streams and in the product

spectra from the reaction of aliphatic -NO<sub>2</sub>-containing compounds in high-temperature water [16]. Most nitriles are industrially produced as intermediates and building blocks in organic synthesis or as organic solvents. Therefore, it is very important to know how fast they hydrolyze because, in this way, waste streams can be cleaned. Hydrolysis of nitriles to amides or carboxylic acids is an important transformation in organic chemistry. Nitrile hydrolysis proceeds in distinct steps under acid or base conditions to achieve carboxamides and then carboxylic acids. Traditionally, hydrolysis of nitriles to the corresponding amides or carboxylic acids is typically carried out in water assisted with a strong acid or base catalyst, making it incompatible with compounds that contain sensitive functional groups [17–19]. Further, these base- or acid-catalyzed reactions have certain limitations and/or disadvantages for the preparation of amides or acids, e.g., the final neutralization of either base or acid leads to unwanted by-products along with large quantities of inorganic salts also with inconvenient product contaminations and pollution effects. In comparison, nitrile hydrolysis assisted with NCW offers a potential for high quality of the reaction products because the by-product formation of inorganic salts can be avoided. Nitriles can be hydrolyzed in NCW or supercritical water without the addition of any catalyst [20–23]. Many research works undertaken on non-catalyzed hydrolysis of nitriles in NCW can be found in the literature, but there is no report on the model compound with -CN at one end and with -CONH<sub>2</sub> at the other end. Previously, we have demonstrated the hydrolysis of iminodiacetonitrile in NCW using a closed batch reactor without the addition of any catalyst. It was found that NCW is an excellent reaction medium for conducting the hydrolysis of nitriles [24].

**Correspondence:** Prof. L.-Y. Dai (lydai@chem.ecnu.edu.cn), Shanghai Key Laboratory of Green Chemistry and Green Process, Department of Chemistry, East China Normal University, Shanghai 200062, P.R. China.

In this work, we have extended the concept of using the same type of batch reactor to study the reactivity of those compounds containing two different types of functional groups, a cyano group and an amide group, in NCW, because this kind of compound can be selectively hydrolyzed to the corresponding cyanocarboxylic acids or diamides, which are indispensable intermediates in the pharmaceutical synthesis industry. 5-Cyanovaleramide (5-CVAM) was selected as a model compound containing those two kinds of functional groups to investigate the hydrolysis reactivity of each of its functional groups and the non-catalyzed kinetics in NCW. 5-CVAM is a starting material for the synthesis of a new DuPont herbicide, azafenidin (Milestone®). The goal of the current work is to contribute quantitative pathways, kinetics, and mechanisms of 5-CVAM to the literature for a better understanding of the hydrolysis of other similar compounds in NCW. Experimental conditions have been undertaken at temperatures ranging from 250 to 310 °C under estimated pressures of 20 MPa for reaction times of 30–120 min.

## 2 Experimental

### 2.1 Materials

5-CVAM (purity  $\geq 98.0\%$ ), 5-cyanovaleric acid (5-CVAC; purity  $\geq 98.0\%$ ), and adipamic acid (ADAA; purity  $\geq 98.0\%$ ) were prepared and purified according to the literature [25, 26]. Adipamide (ADAM; purity  $\geq 99.5\%$ ) and adipic acid (ADA; purity  $\geq 99.5\%$ ) were purchased from Aldrich Chemicals Co. Adiponitrile (purity  $\geq 98.0\%$ ) was commercially available from Alfa Aesar Chemical Co. All the chemicals were used as prepared or received. Freshly double-distilled water was used throughout the experiments.

### 2.2 Procedures

Experiments were conducted in a 316 stainless-steel batch reactor (1.8 cm i.d.  $\times$  6.5 cm length) with a volume of 16.5 cm<sup>3</sup>, which consisted of a body and a fastening cap. A common inlet and outlet was provided for charging and evacuating the reactor, respectively. The temperature of the reaction solution in the reactor was indirectly measured by a thermocouple inserted into a dip nozzle that was installed at about the middle of the reactor as described in the previous publications [24, 27]. The possible maximum working temperature and pressure of this reactor are 450 °C and 45 MPa.

A stock solution of 5-CVAM was prepared by dissolving 5-CVAM in double-distilled water at the desired concentration; the 5-CVAM was completely dissolved under the experimental conditions, ensuring a homogeneous phase in the investigated temperature ranges. The aged reactor was loaded with the stock solution, and the amount of stock solution in the reactor was calculated to drive the pressure inside the reactor to the saturated water vapor pressure at any given temperature. Under the experimental conditions, more than 95% of the reactor volume was

occupied by the liquid phase. As a result, most of the reactant was partitioned into the liquid phase. While estimating the kinetics parameters, this partitioning effect can be duly accounted for. The experimental results would be favorable for obtaining reaction kinetics information within the experimental errors. Prior to each experiment, the reactor was purged with high-purity nitrogen for about 30 min to eliminate any air dissolved in the reaction solution and on top of the reactor. A method of desired pressure control of the reaction system was realized by changing the amount of high-purity nitrogen on top of the reactor. Prior to the hydrolysis experiments, we conducted preliminary experiments to determine a temperature program for achieving the desired value as quickly as possible. The reactor was tightly closed and submerged in a pre-heating molten-salt tank (containing sodium nitrate, potassium nitrate, sodium nitrite) at a certain temperature of 100 °C above the desired temperature. If the pre-heating temperature were set at the desired one, it would take a longer time for the tank to reach the desired temperature because of the heat lost when submerging the reactor. After 5 min (see Fig. 1), the temperature in the reactor could reach the desired temperature, at which point the reaction time is set to zero and the temperature is controlled to keep the reactor within 1 °C of the desired temperature. The temperature inside the reactor was measured instantaneously using a thermocouple ( $\Phi$  1.5 mm) inserted into a dip nozzle inside the reactor and connected to a digital thermometer with a monitor showing the instantaneous change of temperature. At the end of each reaction, the reactor was removed from the molten-salt tank and rapidly quenched in an ice water bath to stop the reaction. The cooled system was first depressurized, and the final reaction mixture was dropped out of the reactor. The reaction contents were recovered by rinsing the reactor with pure water for five times and gathering the final resulting mixture. The uncertainty in these estimated product yields is 95% confidence interval for all of the products, based on five replicate experi-

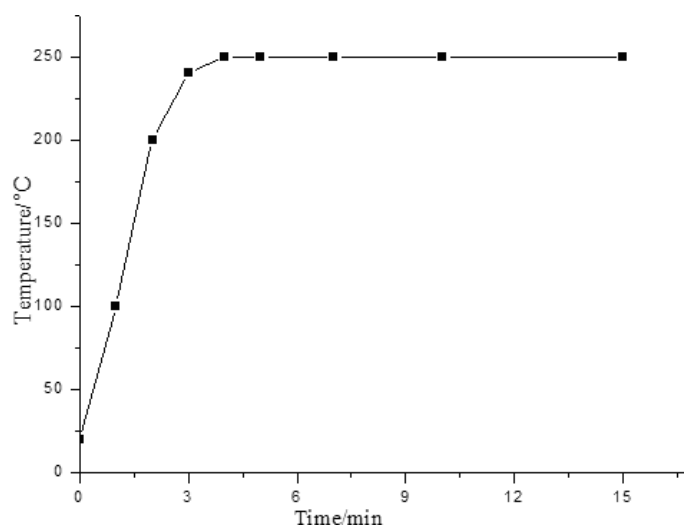


Figure 1. Temperature change in the reactor as a function of time (set temperature of 250 °C).

ments. The points given in the plots with error bars are all the average values of experimental data.

The liquid samples obtained were quantitatively analyzed by a Waters 1525 HPLC instrument equipped with an ODS C<sub>18</sub> 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/L H<sub>3</sub>PO<sub>4</sub> containing 1.1 % vol/vol methanol in water; flow rate of 1.0 mL/min; and a detection wavelength of 200 nm. Product identification was achieved by comparing the results to those for a standard solution of pure compounds and by inspecting HPLC mass spectra.

### 3 Results and Discussion

#### 3.1 Product Identities

Four products resulting from the hydrolysis of 5-CVAM, including ADAM, 5-CVAC, ADAA and ADA, were detected by HPLC (see Fig. 2).

Quantitative analysis of the hydrolysis products was accomplished using a standard calibration curve. Each of the calibration curves was constructed by plotting a linear regression of the average response factor versus the hydrolysis product concentrations for all analyzed calibration standards. Calibration curves were then used to determine the hydrolysis product concentrations in all reference and hydrolyzate samples. Acceptability criteria for identification of individual components in validation studies employing high-purity reference samples required that the retention time for a given hydrolysis product would be within 2 % of the average retention time for each respective standard used to construct the calibration curve for that of the hydrolysis products. Identification of hydrolysis products in hydrolyzate samples was accomplished by inspecting HPLC mass spectra and retention time data with reference standards.

As can be seen in Fig. 2, a lower content of 5-CVAC in the final reaction products was detected under the conditions of high temperature and pressure, possibly because the 5-CVAM

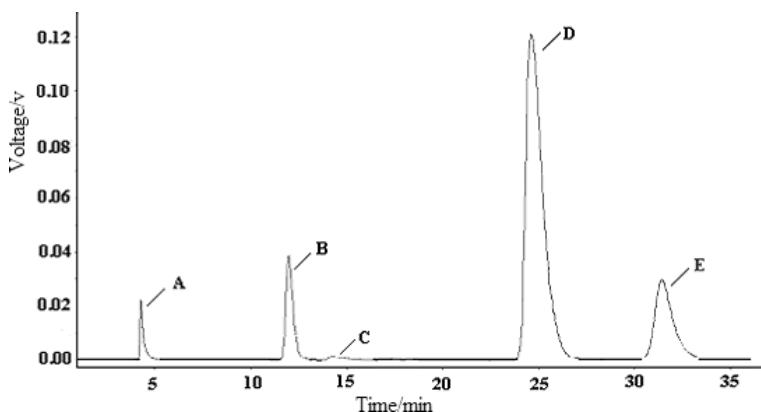
would rather convert to ADAM than to 5-CVAC; therefore, traces of 5-CVAC remained in the products.

#### 3.2 Reaction Scheme

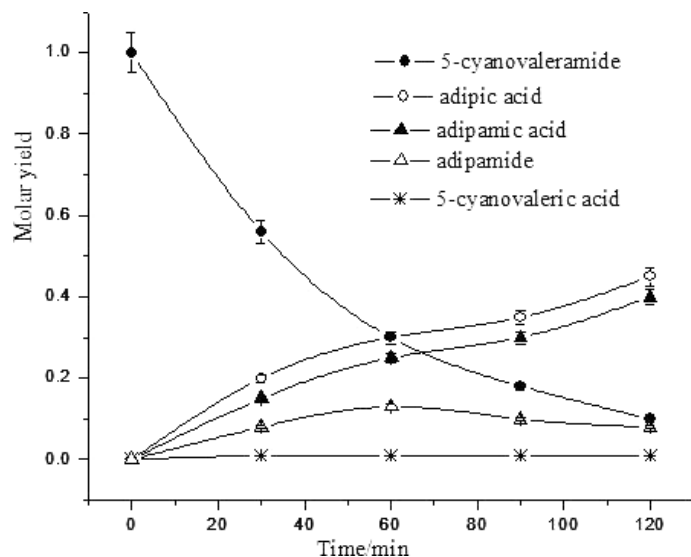
In the overall process of a hydrolysis reaction, a bond in an organic molecule is broken, and an O-H bond in a water molecule also breaks. Then, from the water molecule, an -OH group adds to one part of the organic molecule, and an H atom to the other. Nitrile hydrolysis typically undergoes nucleophilic addition to give products that often undergo a further reaction. For the base-catalyzed hydrolysis of nitriles to carboxylic acids, after OH<sup>-</sup> attack at C, N<sup>-</sup> is protonated. The net of these two steps is the addition of H<sub>2</sub>O across -CN, producing the hydroxy imine, which then tautomerizes to an amide; the amide then undergoes further hydrolysis to the acid.

For the hydrolysis of 5-CVAM, there are two different types of functional groups, a cyano group and an amide group. The amide group is a stronger base than the cyano group. Under the experimental conditions, the concentrations of hydrogen and hydroxyl ion are equal. Depending on the pH, the reaction in aqueous solution may follow different pathways: At high pH the system will follow the so-called “base-catalyzed” route, in which a hydroxyl ion performs a nucleophilic attack on the carbonyl carbon atom next to an amide bond; at low pH, protonation of the carbonyl oxygen atom followed by nucleophilic attack carried out by a water molecule is known as the “acid-catalyzed” pathway [28]. Hydrolysis of nitriles in NCW proceeds basically in terms of the base-catalyzed mechanism because of its lower activation energy [16]. Under basic conditions, it is more difficult to hydrolyze an amide because you need to form a dianion intermediate. Therefore, a nitrile is more easily hydrolyzed to an amide under the basic conditions. Reaction products resulting from the hydrolysis of 5-CVAM were produced as expected, primarily including ADAM, ADAA, ADA, and traces of 5-CVAC. Fig. 3 shows the temporal variations of the molar yields of the major products resulting from the hydrolysis of 5-CVAM in NCW at a temperature of 270 °C. Note that the molar yield is defined here as the ratio of the species concentration to the initial 5-CVAM concentration. The minor product of 5-CVAC presented in Fig. 3 is less than 1.0 mol-%.

Traces of 5-CVAC were detected in the products, suggesting that the cyano group in 5-CVAM is more reactive than the amide group under the same experimental conditions as described in Fig. 2. Obviously, ADAA and ADA were the major reaction products, as their initial rates of appearance matched the initial disappearance of 5-CVAM with a product recovery higher than 90 mol-%. A small amount of ADAM was also detected and formed as a primary intermediate product. The plot shape in Fig. 3 suggests that ADAM undergoes appreciable secondary reactions, possibly hydrolyzing to its subsequent product. In addition, the ADA molar yield increases at the cost of decreasing the molar yields of ADAM and ADAA, because the

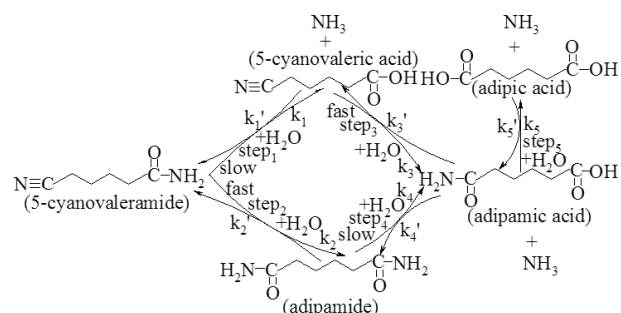


**Figure 2.** Chromatogram of 5-CVAM hydrolysis products in NCW at a temperature of 290 °C, time of 30 min, pressure of 20 MPa. (A) ADA, (B) ADAM, (C) 5-CVAC, (D) 5-CVAM, (E) ADAA.



**Figure 3.** Time dependence of the products spectrum for the reaction of 5-CVAM at 270 °C, 20 MPa.

yield of ADA is always the highest one among all the products. This result also suggests that hydrolysis of 5-CVAM proceeds as a consecutive reaction. Based on the experimental results, a hydrolysis reaction scheme of 5-CVAM in NCW was proposed and is presented in Fig. 4. As can be seen, 5-CVAM will convert to ADAM rapidly through step<sub>2</sub>; step<sub>2</sub> and step<sub>1</sub> are competitive reactions, but step<sub>2</sub> is dominant, because the cyano group in 5-CVAM is easily attacked by hydroxyl ions to form a negative nitrogen ion; then this negative ion captures the proton in water, immediately followed by rearrangement to form ADAM which undergoes similar reaction mechanisms as mentioned above to convert to ADAA. The amide group can also be attacked by a hydroxyl ion to form 5-CVAC. Although 5-CVAC is formed at step<sub>1</sub>, the cyano group in 5-CVAC would be easily attacked by a hydroxyl ion, converting rapidly to ADAA. As a result, traces of 5-CVAC exist in the final products. At the last step (step<sub>5</sub>), the amide group undergoes a similar mechanism as mentioned above to convert to the final product ADA. The yield of ADA is the highest among the hydrolysis products, and it has long-term stability at higher temperature.



**Figure 4.** Hydrolysis reaction scheme of 5-CVAM in NCW.

### 3.3 Reaction Kinetics

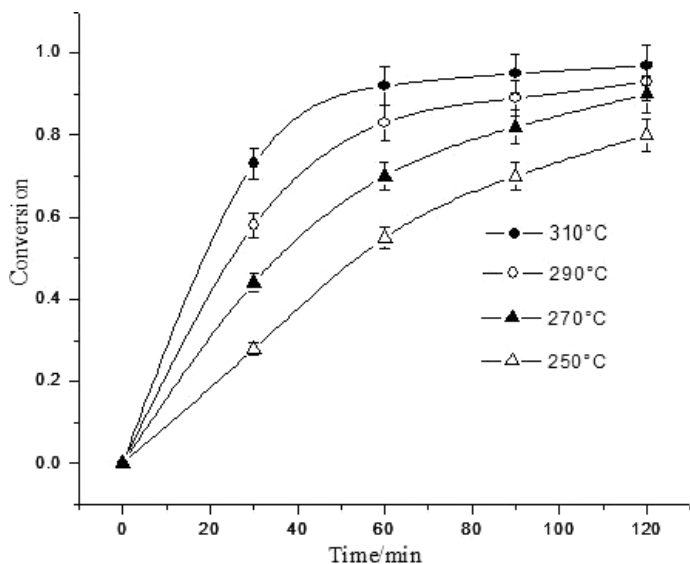
Fig. 5 shows the 5-CVAM molar conversion dependence on time at different temperatures under the estimated pressure of 20 MPa with a reactant concentration of 0.10 mol/L. The uncertainty in these estimated conversions reported herein was 95% confidence interval for all of the products based on five replicate experiments. A complete conversion of 5-CVAM was almost achieved in a reaction time of 120 min at 310 °C. The disappearance rate of 5-CVAM increases considerably with temperature, e.g., a conversion of almost 100% is obtained after 120 min, at a reaction temperature of 310 °C. There is no remarkable increase in the slope of the plot with the accumulation of reaction products in NCW, and therefore no evidence of autocatalysis.

The variation trend of conversion coinciding with the change of reactant concentration is represented by Fig. 6 at a time of 60 min, temperature of 270 °C, with the reactant concentration ranging from 0.04 to 0.16 mol/L. The collision probability between reactant molecules and water molecules increases with increasing reactant concentration for a constant batch reactor volume, resulting in the increase of molar conversion.

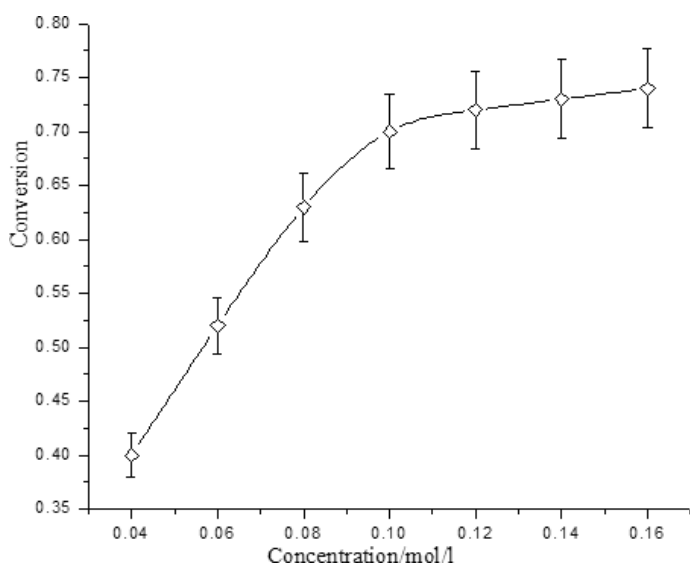
Traditionally, the accumulation of products resulting from the hydrolysis of nitriles has been known to act as the catalytic species to enhance the reaction rate in high-temperature water [16]. This catalytic effect probably exists in the 5-CVAM hydrolysis system, but it is not obvious; the acceleration of the reaction rate due to the accumulation of products is not as great as the collision probability. Fig. 6 shows conclusively that the reaction is not of first order. The conversion increases as the initial reactant concentration increases with all else fixed, so the order must exceed 1. Best-fit model predictions for second-order kinetics were done for the data and are presented in Fig. 7. The kinetics for 5-CVAM shows significant fit of second-order kinetics.

For a better understanding of the hydrolysis reaction kinetics, the relations between 5-CVAM concentration and reaction time were investigated. Best-fit model predictions for second-order reaction kinetics at different temperatures are shown in Fig. 8, where  $k$  is the slope of each plot. If a plot of  $1/C$  vs. time  $t$  produces a straight line with a slope of  $k$  and an intercept of  $1/C_0$ , the reaction will follow second-order reaction kinetics in this reactant. As can be seen, the scattered plots in Fig. 8 are more fitted in a line, with a  $y$ -intercept of  $1/C_{5-CVAM 0}$  of 10 at the initial concentration of 5-CVAM of 0.10 mol/L. Therefore, hydrolysis of 5-CVAM shows coincidence of second-order reaction kinetics in reactant at the investigated temperature ranges. The predicted concentrations of 5-CVAM were in excellent agreement with the additionally verified experimental values, with an average deviation of 2.0% in the investigated temperature range based on second-order reaction kinetics.

The various rate constants at different temperatures are listed in Tab. 1 assumed on second-order reaction kinetics. It is well known that the reaction rate will increase 2–4 orders of magnitude with every increase of 10 °C. Examination of Tab. 1 reveals that the rate constants increase 2–4 orders mag-



**Figure 5.** Reaction kinetics of 5-CVAM in NCW at temperatures of 250, 270, 290, and 310 °C and a pressure of 20 MPa.



**Figure 6.** Conversion dependence on initial reactant concentration at 60 min, 270 °C.

nitide with every increase of 10 °C, suggesting that the rate constant increase is probably due to the increase of temperature and not the autocatalytic effect of the reaction products as proved in Fig. 5. The temperature dependency of the rate constant  $k$  can be described by the Arrhenius equation (Eq. 1):

$$k/\text{L mol}^{-1} \text{ min}^{-1} = A \exp\left(\frac{-E_a}{RT}\right) \quad (1)$$

where  $k$  is the rate constant,  $A$  is the frequency factor or pre-exponential factor,  $E_a$  is the activation energy,  $R$  is the universal gas constant, and  $T$  is the temperature (in Kelvin). The

apparent activation energy of the hydrolysis reaction of 5-CVAM can be calculated according to Eq. (3) using the average rate constants data in Tab. 1. The activation energy and  $\ln A$  were evaluated as averaged 91.84 kJ/mol and 20.0, respectively, in the investigated temperature range. A higher positive activation energy means that a change of the temperature can influence the rate constant, but it is not obvious as approved by the rate constant data in Tab. 1.

**Table 1.** Second-order constants  $k$  ( $\text{L mol}^{-1} \text{ min}^{-1}$ ) for the hydrolysis of 5-CVAM in NCW at temperatures of 250, 270, 290 and 310 °C.

$T$ [°C]	$k$ [ $\text{L mol}^{-1} \text{ min}^{-1}$ ]
250	$0.16 \pm 0.008$
270	$0.42 \pm 0.021$
290	$0.79 \pm 0.039$
310	$1.82 \pm 0.091$

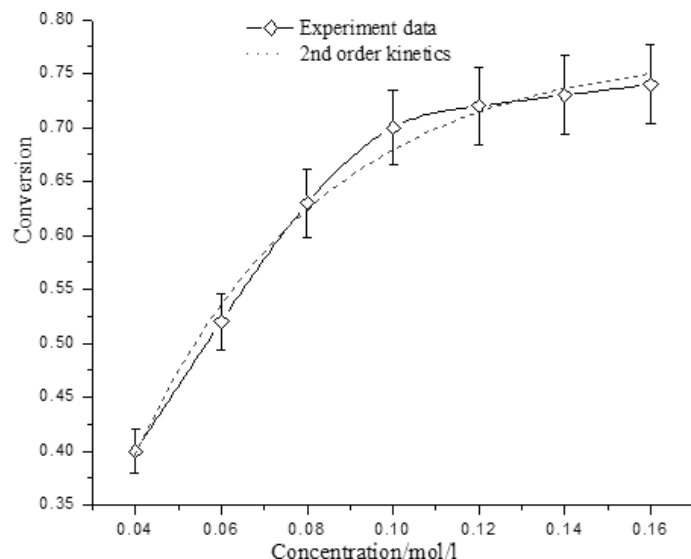
Hydrolysis of 5-CVAM is a multi-step reaction, in which water plays the roles of solvent, reactant and catalyst at the same time. Since water is available in excess, the concentration change of hydrogen or hydroxyl ions can be neglected. Nitriles can be hydrolyzed under acidic or basic conditions; therefore, acid-catalyzed and base-catalyzed mechanisms should exist simultaneously during the nitrile hydrolysis, but the base-catalyzed mechanism is predominant because the activation energy of the base-catalyzed hydrolysis is approximately 21.0 kJ/mol lower than that of the acid-catalyzed hydrolysis [29]. The hydrolysis reaction rate of 5-CVAM in NCW can be described by the following differential equation (Eq. 2) based on the base-catalyzed mechanism according to the reaction scheme in Fig. 4.

$$-\frac{dC}{dt} = kC_{5\text{-CVAM}}^a C_{\text{OH}^-}^b - k_1' C_{5\text{-CVAC}}^c - k_2' C_{\text{ADAM}}^d \quad (2)$$

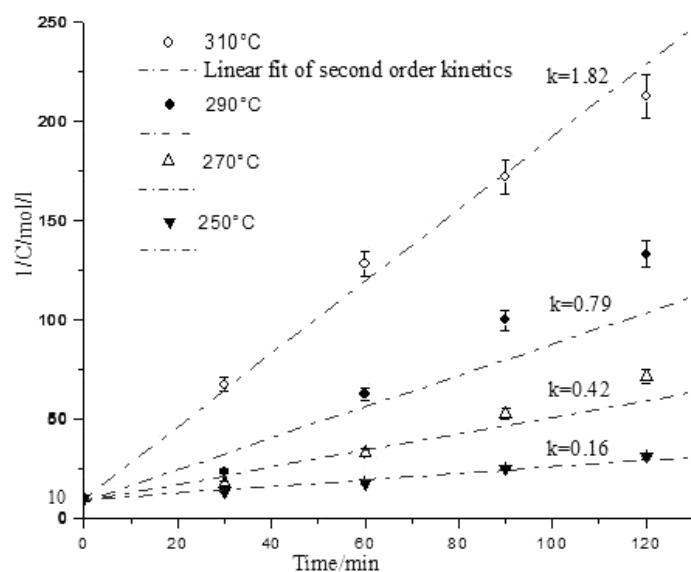
where  $k$ ,  $k_1'$  and  $k_2'$  are the rate constants, and  $k = k_1 + k_2$ ,  $C_{5\text{-CVAM}}$ ,  $C_{\text{OH}^-}$ ,  $C_{5\text{-CVAC}}$  and  $C_{\text{ADAM}}$  are the concentrations of 5-CVAM, hydroxyl ion, 5-CVAC and ADAM in the reaction solution, respectively, and  $a$ ,  $b$ ,  $c$  and  $d$  are reaction orders. As a first approximation, the concentration of  $\text{OH}^-$  in water is a constant because it is in great excess with respect to 5-CVAM. Since the concentration of  $\text{OH}^-$  remains constant, it can be included in the rate constant, wherefore  $kC_{\text{OH}^-}^b$  is approximately considered a constant, and then obtaining a pseudo constant. Supposing that  $k' = kC_{\text{OH}^-}^b$ , Eq. (3) can be derived:

$$-\frac{dC}{dt} = k' C_{5\text{-CVAM}}^a - k_1' C_{5\text{-CVAC}}^c - k_2' C_{\text{ADAM}}^d \quad (3)$$

since 5-CVAM hydrolysis shows second-order reaction kinetics, and then  $a = 2$ . The reaction rate of 5-CVAM is proportional to the concentration square of 5-CVAM. A plot of  $1/C_{5\text{-CVAM}}$  vs. time  $t$  would produce a straight line with a slope



**Figure 7.** Model fit prediction for second-order reaction kinetics for 5-CVAM.



**Figure 8.** Second-order reaction kinetics for 5-CVAM.

of  $k$  and a  $y$ -intercept of  $1/C_{5\text{-CVAM}0}$ , where  $C_{5\text{-CVAM}0}$  is the initial concentration of 5-CVAM. In the investigated temperature range,  $1/C_{5\text{-CVAM}}$  vs. time  $t$  tends to give a straight line, indicating that the hydrolysis reaction with respect to 5-CVAM runs to second-order reaction kinetics in 5-CVAM as described in Fig. 8.

### 3.4 Carbon Balance

On the basis of the experimental results, the carbon balance of the process was determined. It included the carbon content in 5-CVAM, 5-CVAC, ADAM, ADAA and ADA. The quantity of carbon was calculated based on the content of these com-

pounds in the reaction mixture detected by HPLC. Changes of the carbon content for the reaction mixture between particular stages can be observed in Fig. 9. Such a specification of the process enables monitoring of the process and easy comparison of participation of the main substances in the whole hydrolysis. The same type of carbon balance was calculated for all experiments. Due to the possible side reactions, especially in the case of high temperatures and longer reaction times, the average deviation of carbon balance was  $\pm 10\%$ .

## 4 Conclusion

5-CVAM can be hydrolyzed to amide and acid in NCW without the addition of any catalyst. A nearly complete conversion was achieved in a reaction time of 120 min, at a temperature of 310 °C. The relations between 5-CVAM concentration and residence time reveal that hydrolysis of 5-CVAM shows second-order reaction kinetics in the investigated temperature range. Based on the results of the quantitative analysis of the products, a carbon balance was determined, and a possible hydrolysis reaction scheme of 5-CVAM was proposed.

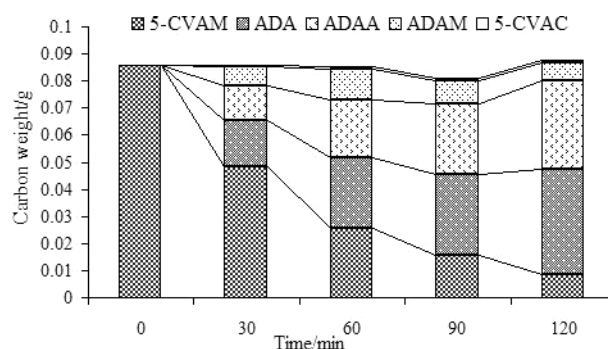
## Acknowledgement

The authors thank the Ministry of Science and Technology of China (grant number: 2007AA05Z101) for financial support. Sincere thanks are due to Prof. Phillip E. Savage coming from the University of Michigan who gave us valuable suggestions on the paper writing.

*The authors have declared no conflict of interest.*

## Symbols used

$A$	$[\text{L mol}^{-1} \text{min}^{-1}]$	pre-exponential factor
$C$	$[\text{mol/L}]$	concentration
$E_a$	$[\text{kJ/mol}]$	activation energy
$K$	$[\text{L mol}^{-1} \text{min}^{-1}]$	reaction rate constant
$P$	$[\text{MPa}]$	pressure



**Figure 9.** Carbon balance for the hydrolysis of 5-CVAM in NCW at a temperature of 270 °C.

R	[J mol <sup>-1</sup> K <sup>-1</sup> ]	molar gas constant
T	[K]	temperature
t	[min]	time

#### Abbreviations

5-CVAC	5-cyanovaleric acid
5-CVAM	5-cyanovaleramide
ADA	adipic acid
ADAA	adipamic acid
ADAM	adipamide
NCW	near-critical water

#### References

- [1] M. Watanabe, T. Sato, H. Inomata et al., *Chem. Rev.* **2004**, *104* (12), 5803.
- [2] N. Akiya, P. E. Savage, *Chem. Rev.* **2002**, *102* (8), 2725.
- [3] H. Weingärtner, E. U. Franck, *Angew. Chem. Int. Ed.* **2005**, *44* (18), 2672.
- [4] A. Kruse, E. Dinjus, *J. Supercrit. Fluids* **2007**, *39* (3), 362.
- [5] J. Dubreuil, M. Poliakov, *Pure Appl. Chem.* **2006**, *78* (11), 1971.
- [6] A. Kruse, E. Dinjus, *J. Supercrit. Fluids* **2007**, *41* (3), 361.
- [7] H. R. Patrick, R. Glaser, K. Griffith et al., *Ind. Eng. Chem. Res.* **2001**, *40* (26), 6063.
- [8] C. M. Comisar, P. E. Savage, *Ind. Eng. Chem. Res.* **2007**, *46* (6), 1690.
- [9] A. Chuntanapum, T. L.-K. Yong, S. Miyake et al., *Ind. Eng. Chem. Res.* **2008**, *47* (9), 2956.
- [10] R. Hashaikh, Z. Fang, I. S. Butler et al., *Fuel* **2007**, *86* (10/11), 1614.
- [11] P. Krammer, H. Vogel, *J. Supercrit. Fluids* **2000**, *16* (3), 189.
- [12] C. M. Comisar, S. E. Hunter, A. Walton et al., *Ind. Eng. Chem. Res.* **2008**, *47* (3), 577.
- [13] S. H. Khajavi, S. Ota, Y. Kimura et al., *J. Agric. Food Chem.* **2006**, *54* (10), 3663.
- [14] S. H. Khajavi, S. Ota, R. Nakazawa et al., *Biotechnol. Prog.* **2006**, *22* (5), 1321.
- [15] G. Orlova, V. Blagojevic, D. K. Bohme, *J. Phys. Chem. A* **2006**, *110* (27), 8266.
- [16] B. Izzo, C. L. Harrell, M. T. Klein, *AIChE J.* **1997**, *43* (8), 2048.
- [17] V. K. Kriable, C. I. Noll, *J. Am. Chem. Soc.* **1939**, *61* (3), 560.
- [18] G. H. Wiegand, M. Tremelling, *J. Org. Chem.* **1972**, *37* (6), 914.
- [19] J. H. Hall, M. Gisler, *J. Org. Chem.* **1976**, *41* (23), 3769.
- [20] A. Krämer, S. Mittelstädt, H. Vogel, *Chem. Eng. Technol.* **1999**, *22* (6), 494.
- [21] E. Venardou, E. Garcia-Verdugo, S. J. Barlow, *Vib. Spectrosc.* **2004**, *35* (1/2), 103.
- [22] C. L. Harrell, J. S. Moscariello, M. T. Klein, *J. Supercrit. Fluids* **1999**, *14* (3), 219.
- [23] Y. B. Tewari, R. N. Goldberg, *J. Chem. Thermodyn.* **2005**, *37* (7), 720.
- [24] P. G. Duan, X. Wang, L. Y. Dai, *Chem. Eng. Technol.* **2007**, *30* (2), 265.
- [25] A. H. Wiley, H. S. Morgan, *J. Org. Chem.* **1950**, *15* (4), 800.
- [26] E. N. Zil'berman, *Zh. Obshch. Khim.* **1955**, *25*, 2127.
- [27] Y. Yang, P. G. Duan, Y. Y. Wang et al., *Chem. Eng. Proc.* **2008**, *47* (12), 2402.
- [28] D. Zahn, *Eur. J. Org. Chem.* **2004**, *19*, 4020.
- [29] B. S. Rabinovitch, C. A. Winkler, *Can. J. Res.* **1942**, *20* (Section B), 185.