Reaction Pathway Analysis of 1-Hexyl Alcohol in Water at Hydrothermal and Supercritical Conditions

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Reactions of 1-hexyl alcohol and acetamide in water at the hydrothermal and supercritical water were conducted using a batch reaction system. A main reaction pathway for the reaction between 1-hexyl alcohol and acetamide was proposed and the optimum reaction conditions where amidation of 1-hexyl alcohol could be occurred in a selective manner were explored. For understanding the effect of additives on the product distribution, reactions of 1-hexyl alcohol and acetamide in the presence of ammonia were also conducted. As a result, it was found that the contribution of amidation to the overall conversion of 1-hexyl alcohol increased by adding ammonia compared with that under ammonia-free conditions.
Key words: Amidation, 1-Hexyl alcohol, Hydrothermal, Supercritical water.

1. INTRODUCTION

Amines are one of important chemicals that have been utilized for medicals, pesticides, surfactants, *etc*. They have been produced from alcohols by the conventional methods as shown in Scheme 1.[1]
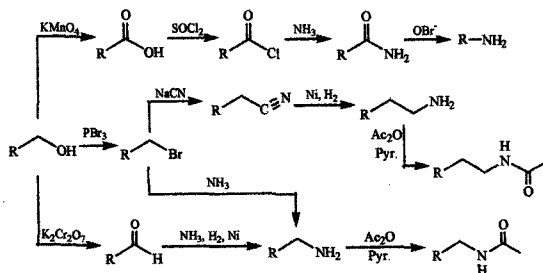
Scheme 1. Conventional production methods for amines and amides[1]

However, these present methods require several reaction steps via halogenation by thionyl chloride (SOCl$_2$) or oxidation/reduction with some catalysts. Because of the formation of halogenide as an intermediate, there are problems in the equipment, or the reaction became a complicated on the oxidation/reduction. From the viewpoint of the green chemistry, it is important that these organic solvents which employed in common processes are alternated to environmentally benign ones.

Water at the near- and supercritical conditions (T$_C$ = 647.2 K, P$_C$ = 22.1 MPa and ρ_C = 0.32 g cm^{-3}) is of importance as a reaction medium because it can create a high conversion process in terms of some unique characteristics of the water at hydrothermal and supercritical conditions. To date, a large number of studies of various chemical reactions in water at the hydrothermal and supercritical conditions have been reported.[2] Especially, Ikushima *et al.*[3] reported that ε-caprolactam could be quantitatively synthesized by the Beckmann rearrangement of cyclohexanone-oxime under a non-catalytic condition in supercritical water. This finding is of great importance to solve the problem of emission of ammonium sulfate, which is a by-product on the conventional synthetic processes, and also to develop an efficient method of ε-caprolactam production. Ito *et al.*[4] studied on the other production method for ε-caprolactam, namely a UCC method[5], in supercritical water. In this method, cyclohexanone is oxidized by the Baeyer-Villiger oxidation to form ε-caprolactone, followed the formation of ε-caprolactam via the reaction between ε-caprolactone and ammonia under a hydrothermal condition. They proposed the main reaction pathway that ε-caprolactone hydrolyzed to 6-hydroxyhexanoic acid and subsequently reacted with ammonia to form 6-hydroxyhexanamide. Also, they found that high yield of ε-caprolactam (87 mol%) was achieved at temperatures of 673-723 K, reaction times of 10-60 minutes and water densities of 0.3-0.5 g cm^{-3}.

An interesting point in the above result is that an amide bond can form by the intramolecular dehydration between a hydroxyl group and an amide group in 6-hexylhexanamide. In general, this reaction does not take place under non-catalytic condition in water. This experimental finding suggests that hydroxyl groups in primary alcohols may directly substitute to amide groups in supercritical water without any catalyst. In this study we conducted experiments of non-catalytic reaction of 1-hexyl alcohol and acetamide in water at hydrothermal and supercritical conditions to propose a

reaction pathway for this reaction. Next, we examined the effect of ammonia on the product distribution of this reaction at the identical conditions.

2. EXPERIMENTS AND ANALYSIS

2.1. EXPERIMENTAL METHODS

Chemicals and their purities used in this experiment are as follows: 1-hexyl alcohol (97+%), hexylamine (98+%), hexanal (95+%), hexene (98+%), hexanoic acid (99+%), hexylacetate (97+%), acetamide (98+%), acetic acid (99.7+%) (Wako Pure Chem. Ind. Co., Ltd.), and aqueous ammonia (Cica-reagent, 29 wt%). N-Hexylacetamide was synthesized from the reaction of hexylamine and acetic anhydrous (Wako Pure Chem. Ind. Co., Ltd., Purity: 99+%) in pyridine.

In this study we employed a batch-type reactor with a volume of 6 cm^3 made of 316 stainless steel tubing (105 mm length, 12.7 mm O.D., and 8.5 mm I.D.). A K-type thermocouple (Sukegawa Electric Ind. Co. Ltd., Model T35-SK-0.75-F-1.6-G-500-2-EXD) was introduced from the end of the 1/16-in.-1/2-in. joint in order to measure an internal temperature of the reactor during the reaction. Prior to an experiment, ultra pure water, 29 wt% aqueous ammonia, acetamide and 1-hexyl alcohol were loaded in the reactor. Then, argon gas was introduced to the reactor inside from the other part of 1/2-in.-1/16-in. joint, which was connected to a bomb of argon gas, and then discharged to the outer system. By repeating this operation several times, air in the reactor was replaced. After finishing the argon substitution, the 1/16-in. union of the reactor was removed from the line of argon gas and a 1/16-in. plug was immediately sealed.

Reaction was initiated by putting into a fluidized sand bath that had set at a reaction temperature in advance. After the desired time has passed, the reactor was taken out from the fluidized sand bath and then put into a water bath to terminate reaction immediately. The reaction time (t) was defined as the time from when the reactor was put into the fluidized sand bath to when it was soaked into water bath. The experimental conditions were in the following: Temperatures between 573-723 K, water densities (ρ) between 0 and 0.5 g cm^{-3}, reaction times between 5 and 60 minutes, initial concentrations of 1-hexyl alcohol of 0.33 mol L^{-1}, acetamide of 1.66-16.8 mol L^{-1}, and ammonia of 0-3.33 mol L^{-1}. After the reaction, liquid portion in the reactor was recovered with washing using ultra pure water and methanol (Wako Pure Chem. Ind. Co., Ltd.; Purity: HPLC grade) in a measuring flask of 50 mL. The conversion of 1-hexyl alcohol (X) and the product yield of i were respectively defined as $X = ([1\text{-hexyl alcohol}]_0 - [1\text{-hexyl alcohol}])/[1\text{-hexyl alcohol}]_0)$ and the yield of $i = [i]/[1\text{-hexyl alcohol}]_0$. The product selectivity of i was also calculated as the ratio of the yield of i to X.

2.2. ANALYTICAL METHODS

Products in the liquid portion was identified by a gas chromatography mass spectroscopy (GC-MS) (Hewlett Packard; Model HP 5890 series) and quantified by a GC with a flame ionization detector (GC-FID) (Hewlett Packard, Model HP6890 Series GC system) and a high-performance liquid chromatography (HPLC) (JASCO) with a refractive index (RI) detector (JASCO, Model RI-2031). The GC analyses were performed at the following conditions; Column: HP-5 (60 m×φ0.32 mm×1.0 μm); Carrier gas: High purity He gas (Nippon

Sanso, Co., Ltd.); Sprit ratio: 1:50; Injection temperature: 573 K (473 K in GC-MS); Detection temperature: 573 K (473 K in GC-MS). A filament current and a voltage of the light doubling tube were 300 μA and 700 mV, respectively. The temperature profile of the GC-FID was as follows. At first, the temperature of the column was kept at 313 K for 10 min, elevated to 373 K at a heating rate of 20 K/min and further heated up to 473 K at 5 K/min, and finally kept at 473 K for 7 min. The temperature profile of the GC-MS was as follows. The temperature of the column was kept at 313 K for 10 min, elevated to 473 K at 5 K/min and then kept at 473 K for 10 min. The HPLC analysis was performed at the following conditions; Column: KC-811 (Shodex), Temperature: 313 K; Solvent: 0.1 % H_3PO_4 aqueous solution; Flow rate: 1.0 cm^3 min^{-1}.

3. RESULTS AND DISCUSSION

Fig. 1 shows the yield of the main products derived from 1-hexyl alcohol at 673 K, 0.5 g cm^{-3}, and $[\text{acetamide}]_0 = 1.66$ mol L^{-1}. Products identified in this study were N-hexylacetamide, hexanal, hexene, hexylamine, hexylacetate, acetic acid, and hexanoic acid. The X increased with time and reached over 60 % at 60 minutes. The N-hexylacetamide yield was 21.9 % at 60 minutes. The hexana yield became about 20 % at 30 minutes and decreased with time. The hexene yield maximized (8.0 %) at 30 minutes and then decreased with time. The hexylacetate yield was 4.4 % at 10 minutes and then decreased to 0.8 % at 60 minutes. The yield of hexylamine, a hydrolysis product of N-hexylacetamide, was low (1.5 %), although it was expected that N-hexylacetamide easily hydrolyzed to hexylamine in supercritical water. The reason for the low level of hexylamine may be that N-hexylacetamide is stablized over hexylamine due to solvation in supercritical water, or that N-hexylacetamide is converted to 1-hexyl alcohol and acetic acid by the reverse reaction of amidation. Under the employed reaction conditions, about 70 % of acetamide hydrolyzed to form acetic acid at 10 minutes, and the yield of acetic acid scarcely changed even for extended reaction times. In summary, amidation between 1-hexyl alcohol and acetamide occurred in supercritical water. Moreover, we evaluated any possibility of the formation of
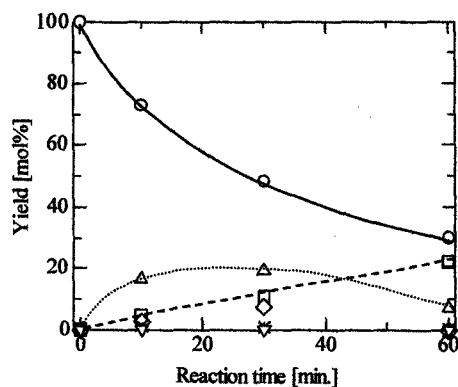

Fig.1 Yields of the main products at 673 K, 0.5 g cm^{-3}, and $[1\text{-hexyl alcohol}]_0 = 0.33$ mol L^{-1}.

Symbols: O, 1-hexyl alcohol; □, N-hexylacetamide;
△, hexanal; ◇, hexene; ×, hexylamine; +, hexylacetate;
▽, hexanoic acid.

N-acetylacetamide and/or hexylamine from the reaction between acetamide and hexene in subcritical and supercritical water and confirmed that they did not form under this condition.

On the basis of the results, we proposed a main reaction pathway for this system in water at hydrothermal and supercritical conditions. Main reaction paths are a) the intermolecular dehydration between 1-hexyl alcohol and acetamide, b) reverse Cannizzaro reaction between 1-hexyl alcohol and acetic acid formed by the dissociation of acetamide, c) the intramolecular dehydration to hexene, d) the intermolecular dehydration (esterification) between 1-hexyl alcohol and acetic acid, and e) hydrolysis of acetamide to ammonia and acetic acid. It has been already reported that the Cannizzaro reaction occurs in supercritical water under catalyst free conditions.[6] We also found that the reverse Cannizzaro reaction can take place in supercritical water from a preliminary experiment.[5]

Next, we evaluated the effect of ammonia on the reaction of 1-hexyl alcohol and acetamide in supercritical water. Reaction condition was set at 673 K, 0.5 g cm^{-3}, 0-60 minutes, [1-hexyl alcohol]$_0$ = 0.33 mol L^{-1}, [acetamide]$_0$ = 1.65 mol L^{-1} and [ammonia]$_0$ = 1.66 mol L^{-1}. Fig. 2(a) and 2(b) show the variations of the main products with or without ammonia, respectively. At 60 minutes, the X was about 10 % lower than that in the absence of ammonia (Fig. 2(b)). The Y_S increased with time and reached 43.4 % (selectivity: 69.4 %) at 60 minutes. This value was much higher than that obtained under an ammonia free
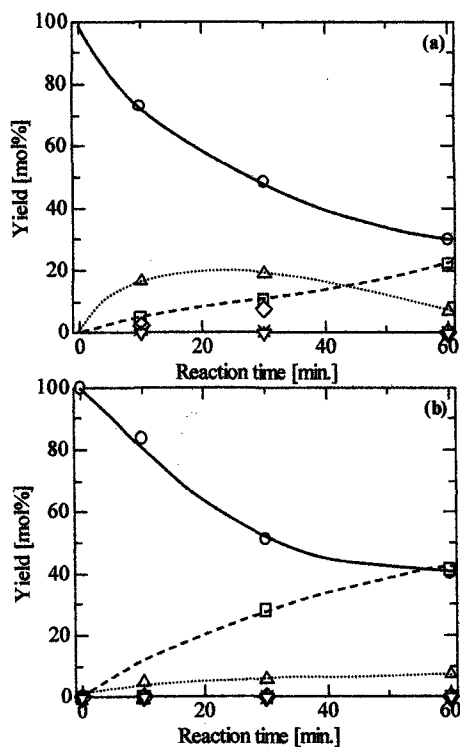
condition (21.9 %). The yield of hexene was lowered to 5-7 %, which was less by one third compared with that obtained in the absence of ammonia. Also, no formation of hexylamide was confirmed. Additionally, hexene, which was a product of intramolecular dehydration of 1-hexyl alcohol, did not form under these conditions. This is probably because intramolecular dehydration of 1-hexyl alcohol is inhibited under alkali conditions. From this result, we found that addition of ammonia suppressed both the reverse Cannizzaro reaction and the intramolecular dehydration, resulting in a great increase in the product selectivity for *N*-acetylacetamide.

The effect of concentration of ammonia on the reaction between 1-hexyl alcohol and acetamide was also investigated. Fig. 3 shows the plot of the selectivity of i and the X versus [ammonia]$_0$ at 673 K, 0.3 g cm^{-3}, 60 minutes, [1-hexyl alcohol]$_0$ = 0.33 mol L^{-1}, and [acetamide]$_0$ = 1.65 mol L^{-1}. The X was 37.4 % under an ammonia free condition, but gradually decreased to 21.4 % increase of [ammonia]$_0$. The reason why the X decreased with an increase of concentration of ammonia is probably because 1-hexyl alcohol is more stable under alkali conditions than under neutral or acidic conditions. The selectivity of *N*-acetylacetamide was 13.5 % at [ammonia]$_0$ = 0 and dramatically increased (46 %) at [ammonia]$_0$ = 1.0 mol L^{-1}. The higher the [ammonia]$_0$ increased from 1.0 to 3.33 mol L^{-1}, the larger the selectivity of *N*-acetylacetamide became up to 55 %. When ammonia was inserted in the reaction system, the selectivity of hexanal became lower than that without ammonia, but increased with an increase of [ammonia]$_0$. Although a main reason for this result may relate to the pH of the reaction environment. A clear rationale for these results cannot be offered. From these experimental results, it was shown that the appearance of ammonia in the reaction system lead to the decrease in the conversion rate of 1-hexyl alcohol, and also the promotion of amidation of 1-hexyl alcohol to *N*-acetylacetamide. This result probably originates from the fact that the structural stabilities of both 1-hexyl alcohol and acetamide become higher than under neutral and acidic conditions.
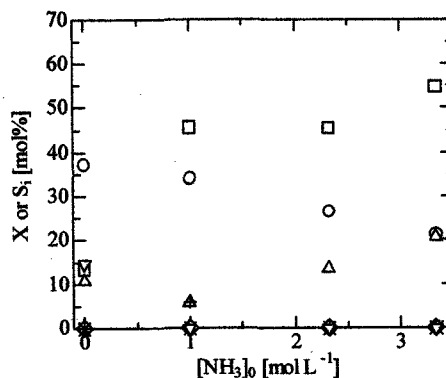

Fig.2 Effect of ammonia on the yields of main products at 673 K, 0.5 g cm^{-3}, and [1-hexyl alcohol]$_0$ = 0.33 mol L^{-1}:
(a) without NH$_3$; (b) [NH$_3$]$_0$ = 1.65 mol L^{-1}.
Symbols: O, 1-hexyl alcohol; □, *N*-hexylacetamide; △, hexanal; ◇, hexene; ×, hexylamine; +, hexylacetate; ▽, hexanoic acid.

Fig.3 Effect of ammonia concentration [NH$_3$]$_0$ on the product distributions at 673 K, 0.5 g cm^{-3}, and [1-hexyl alcohol]$_0$ = 0.33 mol L^{-1}: (a) without NH$_3$; (b) [NH$_3$]$_0$ = 1.65 mol L^{-1}.
Symbols: O, 1-hexyl alcohol; □, *N*-hexylacetamide; △, hexanal; ◇, hexene; ×, hexylamine; +, hexylacetate; ▽, hexanoic acid.

The effect of reaction temperature for the reaction was also investigated at the condition of $[1\text{-hexyl alcohol}]_0 = 0.33$ mol L^{-1}, $[\text{acetamide}]_0 = 1.66$ mol L^{-1} and 0.3 g cm^{-3}. Table I shows the results at 573 and 673 K in the absence/presence of ammonia. At 573 K, the product distribution in the presence of ammonia was similar to that in the absence of ammonia, while at 673 K the N-hexylacetamide yield increased to 86.7 % compared with the corresponding result under ammonia free conditions (74.5 %). It is well known that amides can easily hydrolyze under hydrothermal and supercritical conditions.[7] From these preliminary experiments we actually confirmed that N-hexylacetamide rapidly converted to hexylamine and acetic acid via hydrolysis in near- and supercritical water without acid and ammonia.[5] This suggests that primary amines can be produced by two steps from primary alcohols using near- and supercritical water.

Table I. Comparison of product distribution on amidation in the absence/presence of ammonia at 573 K and 673 K, $[1\text{-hexyl alcohol}]_0 = 0.33$ mol L^{-1}, $[\text{ammonia}]_0 = 16.6$ mol L^{-1}, 0.3 g cm^{-3}, and 60 minutes.

T K	$[NH_3]_0$ mol L^{-1}	$100\text{-}X$ mol%	Yield / mol%*			
			1	2	3	4
573	1.66	63.1	12.8	13.2	4.7	6.5
	0.00	60.8	11.3	11.3	4.0	7.1
673	1.66	4.0	86.7	14.9	n.d.	2.0
	0.00	3.6	74.5	9.6	n.d.	2.0

* 1: N-Acetylacetamide; 2: hexanal; 3: hexylamine; 4: hexanoic acid.

Finally, a reaction pathway for the reaction of the 1-hexyl alcohol/acetamide/ammonia system in subcritical and supercritical water is summarized as Scheme 2. By adding ammonia in the reaction system, dissociation of acetamide is suppressed and therefore the reaction between 1-hexyl alcohol and hexanal is inhibited. As a result, amidation of 1-hexyl alcohol to ammonia can selectively take place in supercritical water, followed the formation of hexylamine via hydrolysis of ammonia.
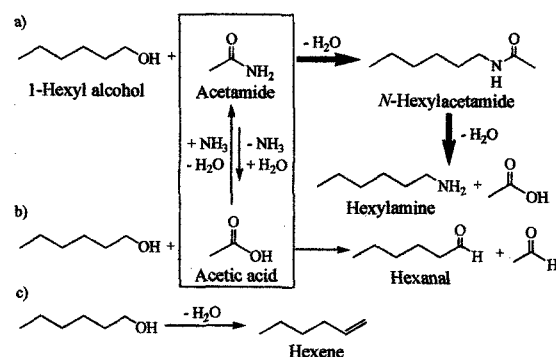
Scheme 2. The reaction pathway for 1-hexyl alcohol-acetamide-ammonia-water system under hydrothermal and supercritical conditions. Each elemental reaction path is as follows: a) amidation; b) reverse Cannizzaro reaction; c) intramolecular dehydration.

4. CONCLUSIONS

In summary, we have presented the effect of ammonia for the reaction between 1-hexyl alcohol and acetamide

in subcritical and supercritical water. We could find reaction conditions for the efficient production of N-hexylacetamide in water at the supercritical condition. This experimental finding is of great importance for developing a new method that can produce primary amides from primary alcohols. Moreover, it was suggested that primary amines could be produced from primary alcohols by only two simple steps in near- and supercritical water. Future efforts will be directed toward conducting the kinetic and mechanistic study on this reaction and for determining an optimum condition where primary amides and amines can be efficiently recovered.

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