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Efficient and Eco-Friendly Anionic Polymerization of Acrylamide under Microwave Irradiation and Hydrolysis of the Obtained Polymers by Microwave Irradiation

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ABSTRACT: The polymerization of acrylamide was carried out using *t*-BuOK as an initiator in DMF under microwave irradiation. As a result, poly(β-alanine) was obtained in a good yield. With 100 W, 2.45 GHz microwave irradiation, the formation of polymer was accelerated. Furthermore, the hydrolysis of poly(β-alanine) was carried out using acids or bases under microwave irradiation. When poly(β-alanine) was hydrolyzed at 100 °C for 3 h with NaOH or KOH, the degree of hydrolysis reached 68−71%. When poly(β-alanine) was hydrolyzed at 100 °C for 3 h with HCl or H_2SO_4, the degree of hydrolysis reached 64−76%.

Introduction

In recent years, due to increasing environmental concern, green chemistry has been receiving progressively more attention since the 1990s.[1−3] Therefore, there is a great necessity for the advancement of novel methodologies for chemical reactions using an environmentally eco-friendly method. A promising approach from this standpoint is to search for new processes and technologies which, from the very beginning, are aimed at sharply curtailing environmental pollution by reducing the volumes of chemical production wastes.

Microwave irradiation has been applied to various chemical reactions. Many review papers were published about microwave-assisted chemical reactions.[4−7] The microwave method provides a fast and direct heating method. In many cases, it can dramatically reduce reaction times from hours to minutes, increase product yields, and enhance product purity.[8,9] Microwaves heat up reaction mixtures by following two heating methods.[5]

One is the dipolar polarization method. When a substance is irradiated with microwaves, it has a dipolar moment. A dipole will align itself with the microwave field by rotation. In liquids, the presence of closely neighboring molecules stops this alignment from being instantaneous. In the microwave region of the electromagnetic spectrum, the frequency of the applied irradiation is low enough so that the dipoles have time to respond to the alternating electric field and therefore rotate. However, the frequency is not high enough for the rotation to precisely follow the field. Therefore, the dipole reorientates to align itself with the electric field, but the field is already changing, and this generates a phase difference between the orientation of the field and that of the dipole. This phase difference causes energy to be lost by molecular friction and collisions, giving rise to dielectric heating. Because of the nature of microwave heating, if a reaction is carried out in a solvent, the medium or reactants need to have high dielectric constant (ε) in order to benefit from microwave heating.

Another method is the conduction method. Microwave irradiation of a solution containing ions in the sample will make the ions move through the solution under the influence of the electric field applied, resulting in an expenditure of energy due to an increased collision rate, thus converting kinetic energy into heat. This effect is particularly important at higher temperatures. When liquids containing ions are applied under microwave irradiation, this method will predominate.

Polar solvents such as 1-methyl-2-pyrrolidone ($\varepsilon = 32.2$), dimethyl sulfoxide ($\varepsilon = 46.7$), and *N*,*N*-dimethylformamide (DMF) ($\varepsilon = 36.7$) get warm efficiently under microwave irradiation. From the above-mentioned ε, probably amide compounds such as acrylamide will have a very high dielectric constant. Therefore, it is expected that the polymerization of acrylamide will proceed very efficiently. Generally, vinyl monomers having active hydrogens such as acrylamide are known to undertake hydrogen-transfer polymerization under basic conditions to give rise to polymers possessing functional groups in the main chain. This system was first patented in 1954 by Matlack[10] and published in 1957 by Breslow et al.,[11] in which they described that poly(β-alanine) was obtained. Since the propagating N-anions derived from acrylamide are also ionicity, it is expected that hydrogen-transfer polymerization will proceed very efficiently under microwave irradiation.

Until now, the microwave-assisted hydrolysis of amide compounds has been tried.[12,13] From this knowledge, it is expected that the hydrolysis of poly(β-alanine) proceed effectively to give β-alanine under microwave irradiation. β-Alanine is a β-amino acid in which the amino group is at the β-position from the carboxylate group. In recent years, there has been increasing interest in new design and construction of novel synthetic peptides that mimic a protein's secondary structure, i.e., turns, helices, and sheets.[14] For example, homopeptides of β-peptide can adopt stable 14 helical secondary structures in aqueous solution.[15−18] Schepartz et al. reported that homopeptides of β-peptide can assemble into defined, cooperatively folded, quaternary structures and constitutes an important step toward designing protein-like assemblies from non-natural polymers. Moreover, β-peptide dimers stabilized covalently by a disulfide bond[19] or noncovalently by Watson−Crick base pairing[20] as well as self-assembling β-peptide nanotubes[21] have been reported. From a chemical recycling viewpoint, it may be meaningful that

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β-amino acid, which is a useful building block can be obtained by the microwave-assisted hydrolysis of poly(β-alanine). Herein, we wish to describe the result of anionic polymerization of acrylamide under microwave irradiation. We also describe studies on the hydrolytic properties of poly(β-alanine) under microwave irradiation.

Experimental Section

Materials. Acrylamide (AAm) was recrystallized from benzene. 2,2′-Azobis(isobutylronitrile) (AIBN) was recrystallized from ethanol. All other solvents and reagents were purchased from Wako Pure Chemical Industries, Ltd. Poly(acrylamide) obtained by radical polymerization was prepared by a previously reported procedure.[22]

Measurements. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECA-500 spectrometer. IR spectra were measured on a JASCO FT/IR-4200 spectrometer. The viscosity of polymer was measured in 90% formic acid at 30 °C with an Ostwald viscometer.

Microwave Irradiation. Microwave irradiation experiment was performed using an EYELA Wave Magic MWO-1000S, equipped with a magnetron (2.45 GHz, 500 W). The reaction was carried out in a 30 mL three-necked test tube at the center of a microwave oven.

Anionic Polymerization of AAm under Mircowave Irradiation. To a 30 mL three-necked test tube equipped with a reflux condenser containing a DMF (35 mL) solution of acrylamide (5.21 g, 73.30 mmol) and *N*-phenyl-β-naphthylamine (1 mol %) as a radical inhibitor, potassium *tert*-butoxide (3 mol %) was added as an initiator. The reaction mixture was 100 W microwave irradiated. After irradiation for 100−180 s, the reaction mixture was poured into acetone, and the precipitated polymer was purified with boiling acetone by a Soxhlet extractor for 48 h and dried at 60 °C in vacuum for 48 h. IR (KBr): 3449, 3294, 3089, 2943, 2895, 1643, 1547, 1433, 1367 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.60−2.80 (m, 2H, $-CH_2-C\mathit{H}_2-CO-$), 3.25−3.99 (m, 2H, $-N-C\mathit{H}_2-CH_2-$), 7.48 ppm (s, 1H, $-CO-N\mathit{H}-$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 30.85, 34.01, 36.45, 36.70, 176.12 ppm.

Anionic Polymerization of AAm by Conventional Heating. To a 30 mL three-necked test tube equipped with a reflux condenser containing a DMF (7.0 mL) solution of acrylamide (1.00 g, 14.07 mmol), and *N*-phenyl-β-naphthylamine (1 mol %) as a radical inhibitor, potassium *tert*-butoxide (3 mol %) was added as an initiator. After being stirred at 130 °C for 1.5 h under usual atmospheric conditions, the reaction mixture was poured into acetone. The precipitated polymer was purified with boiling acetone by a Soxhlet extractor for 48 h and dried at 60 °C in vacuum for 48 h. IR (KBr): 3450, 3292, 3090, 2941, 2892, 1654, 1542, 1431, 1371 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.60−2.80 (m, 2H, $-CH_2-C\mathit{H}_2-CO-$), 3.25−3.99 (m, 2H, $-N-C\mathit{H}_2-CH_2-$), 7.46 ppm (s, 1H, $-CO-N\mathit{H}-$). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 30.87, 35.23, 36.75, 174.64 ppm.

Hydrolysis of Poly(β-alanine) under Microwave Irradiation. Poly(β-alanine) (100 mg), which was synthesized by microwave irradiation, was dissolved in distilled water (8.5 mL) at 60 °C in a two-necked test tube. After 1 h, 11.5 mL of an acid (6 N HCl, or 6 N H_2SO_4 aqueous solution) or a base (6 N NaOH, or 6 N KOH aqueous solution) solution was added to poly(β-alanine) solution at room temperature. A 100 W microwave irradiated the reaction mixture at 100 °C in the temperature control mode. After irradiation for 1.0−3.0 h, the reaction mixture was neutralized by 6 N HCl or 6 N NaOH aqueous solution. The neutralized solution was diluted with D_2O. Then the solution was transferred to an NMR tube. The degree of hydrolysis was estimated by NMR measurements.

Hydrolysis of Poly(β-alanine) by Conventional Heating. Poly (β-alanine) (100 mg), which was synthesized by microwave irradiation, was dissolved in distilled water (8.5 mL) at 60 °C in a two-necked test tube. After 1 h, 11.5 mL of an acid (6 N HCl or 6 N H_2SO_4 aqueous solution) or a base (6 N NaOH, or 6 N KOH aqueous solution) solution was added to poly(β-alanine) solution at room temperature. After conventional oil bath heating for 0.5−3.0 h, the reaction mixture was neutralized by 6 N HCl or 6 N NaOH aqueous solution. The neutralized solution was diluted with D_2O. Then the solution was transferred to an NMR tube. The degree of hydrolysis was estimated by NMR measurements.

Hydrolysis of *N*-Methlypropionamide under Microwave Irradiation. *N*-Methlypropionamide (100 mg) was dissolved in distilled water (8.5 mL) in a two-necked test tube. After the dissolution of poly(β-alanine), 11.5 mL of acid (6 N HCl or 6 N H_2SO_4 aqueous solution) or base (6 N NaOH or 6 N KOH aqueous solution) solution were added to *N*-methlypropionamide solution at room temperature. The reaction mixture was irradiated with 100 W microwaves at 100 °C (in 6 N HCl or 6 N H_2SO_4 aqueous solution) or 50 °C (in 6 N NaOH or 6 N KOH aqueous solution) in the temperature control mode. After irradiation for 1.0−3.0 h, the reaction mixture was neutralized by 6 N HCl or 6 N NaOH aqueous solution. The neutralized solution was diluted with D_2O. Then the solution was transferred to an NMR tube. The degree of hydrolysis was estimated by NMR measurements.

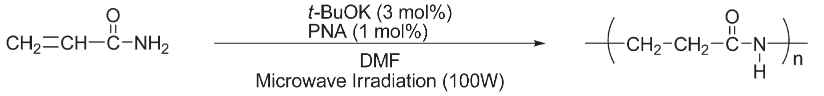
Hydrolysis of *N*-Methlypropionamide by Conventional Heating. *N*-Methlypropionamide (100 mg) was dissolved in distilled water (8.5 mL) in a two-necked test tube. After the dissolution of poly(β-alanine), 11.5 mL of acid (6 N HCl or 6 N H_2SO_4 aqueous solution) or base (6 N NaOH or 6 N KOH aqueous solution) solution were added to *N*-methlypropionamide solution at room temperature. After the conventional oil bath heating for 0.5−3.0 h, the reaction mixture was neutralized. The neutralized solution was diluted with D_2O. Then the solution was transferred to an NMR tube. The degree of hydrolysis was estimated by NMR measurements.

Results and Discussion

Anionic Polymerization of AAm under Mircowave Irradiation. To evaluate the effect of microwave irradiation time, the polymerization of AAm was carried out with different irradiation time (Scheme 1). Polymers were obtained in 39−96% yield as an acetone-insoluble part (Table 1). With an increase in microwave irradiation time, the yields of polymers increased. Moreover, the viscosities of the obtained polymers increased with an increase in microwave irradiation time. Compared to conventional oil bath heating, the microwave-assisted polymerization reaction shortened the reaction time to about 1/30. It can be concluded that the polymers grew by microwave irradiation.

From the ^{1}H NMR spectra of all the polymers obtained, hydrogen-transfer polymerization was found to proceed exclusively irrespective of the irradiation time. The representative ^{1}H NMR spectrum of the obtained polymer is shown in Figure 1a, in which peaks attributable to the methylenes adjacent to the nitrogen atom and those adjacent to the carbonyl group were observed at δ 3.25−3.99 (b) and

Scheme 1. Anionic Polymerization of AAm under Microwave Irradiation



$$CH_2{=}CH-\overset{O}{\overset{\|}{C}}-NH_2 \xrightarrow[\text{DMF, Microwave Irradiation (100W)}]{t\text{-BuOK (3 mol\%), PNA (1 mol\%)}} \left(CH_2-CH_2-\overset{O}{\overset{\|}{C}}-\underset{H}{N} \right)_n$$

Table 1. Anionic Polymerization of Acrylamide under Microwave Irradiation

run	reaction time	temperature (°C)	yield (%)	η_{sp}
1	100 s	78	39	0.05
2	120 s	84	40	0.04
3	140 s	108	55	0.07
4	160 s	112	57	0.08
5	180 s	130	96	0.21
6	40 min	78	82	0.01
7	50 min	108	87	0.13
8	90 min	78	85	0.05
9	90 min	108	93	0.18
10	90 min	130	96	0.24

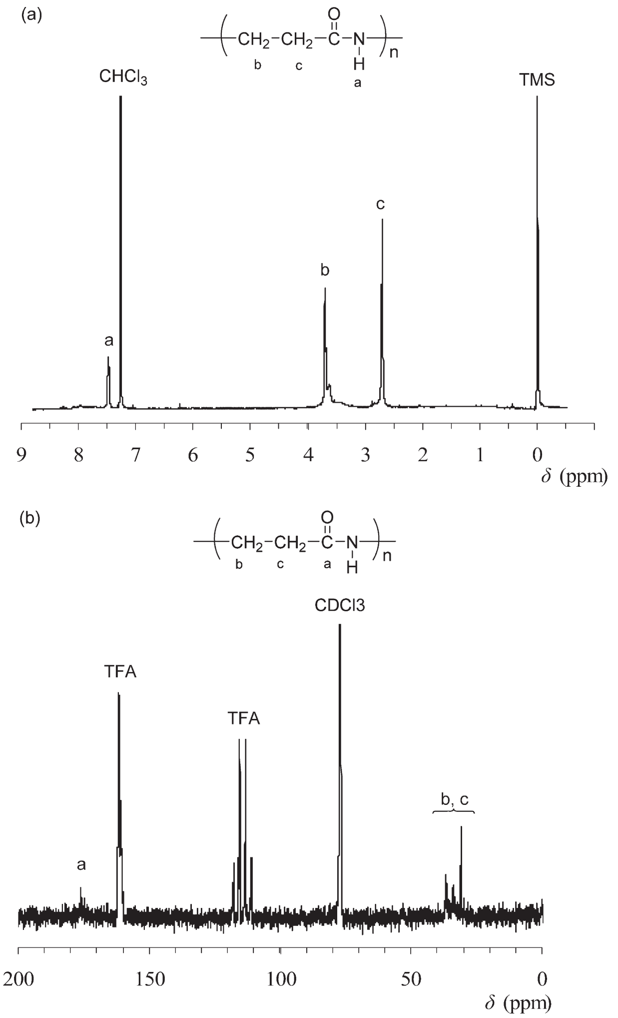


Figure 1. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of the polymer by anionic polymerization under microwave irradiation in $CDCl_3$/TFA (v/v = 4/1).

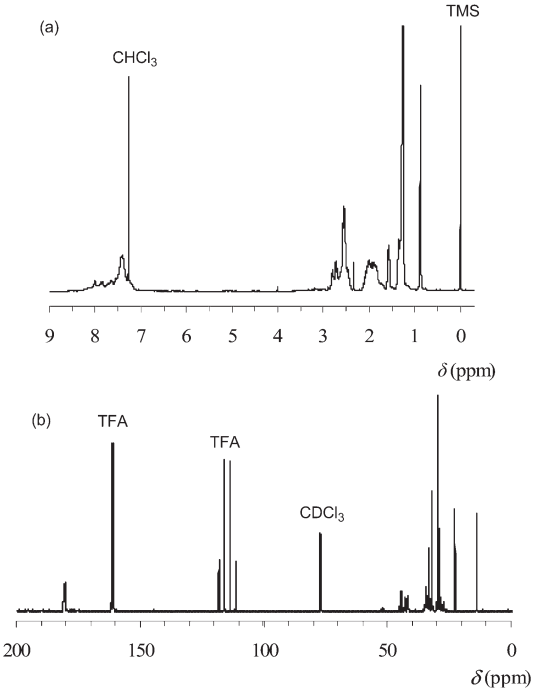


Figure 2. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of poly(acrylamide) by radical polymerization in $CDCl_3$/TFA (v/v = 4/1).

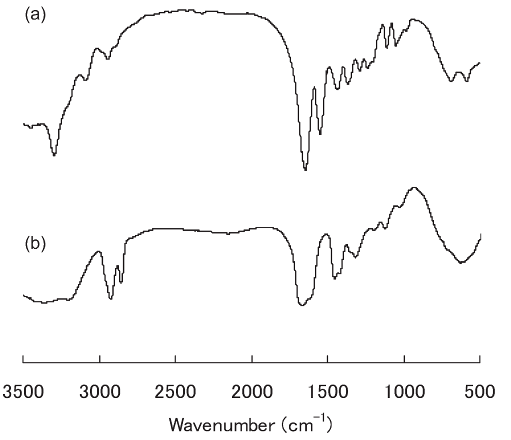


Figure 3. IR spectra of the polymer obtained by microwave irradiation (a) and poly(acrylamide) obtained from radical polymerization (b).

2.70 (c) ppm, respectively. From the ^{1}H NMR spectra of the obtained polymers, the hydrogen-transfer polymerization was found to proceed exclusively. Consequently, poly(β-alanine) was obtained by microwave irradiation. However, the possibility of partial vinyl polymerization could not be excluded. Thus, poly(acrylamide) was prepared independently by radical polymerization, and its ^{1}H NMR spectrum was used as a reference. In this case, the peaks due to the methylene and methine protons (c′ and b′) were observed at δ 1.50−2.20 and δ 2.37−2.66 ppm, respectively (Figure 2a), although the former cannot be seen in Figure 1a. Additionally, in the ^{13}C NMR spectrum of the radically polymerized poly(acrylamide), the peaks due to methine carbon (b′) were observed at δ 41−46 ppm in Figure 2b.[23] On the other hand, the peaks resulting from radical polymerization were not detected in the polymer prepared by the microwave-assisted anionic polymerization (Figure 1b).

The FT-IR spectra of the obtained polymers are shown in Figure 3. The IR spectrum of the poly(acrylamide) obtained by radical polymerization showed an absorption band at 1665 cm^{-1} based on the C=O stretching frequency (Figure 3b). In the IR spectrum of the polymer by microwave irradiation, the absorption band based on poly(acrylamide) was not observed at 1665 cm^{-1} (Figure 3a). In the case of the polymer by microwave irradiation, the C=O stretching frequency was observed at 1643 cm^{-1}.

Hydrolysis of Poly(β-alanine) under Microwave Irradiation. We employed poly(β-alanine) which was prepared by the conditions detailed in Table 1 (run 5) for the hydrolysis experiments. An aqueous solution of poly(β-alanine) with a base or acid was 100 W microwave irradiated at 100 °C for 1−3 h in the temperature control mode (Scheme 2). The hydrolysis of poly(β-alanine) mainly gives β-alanine. The

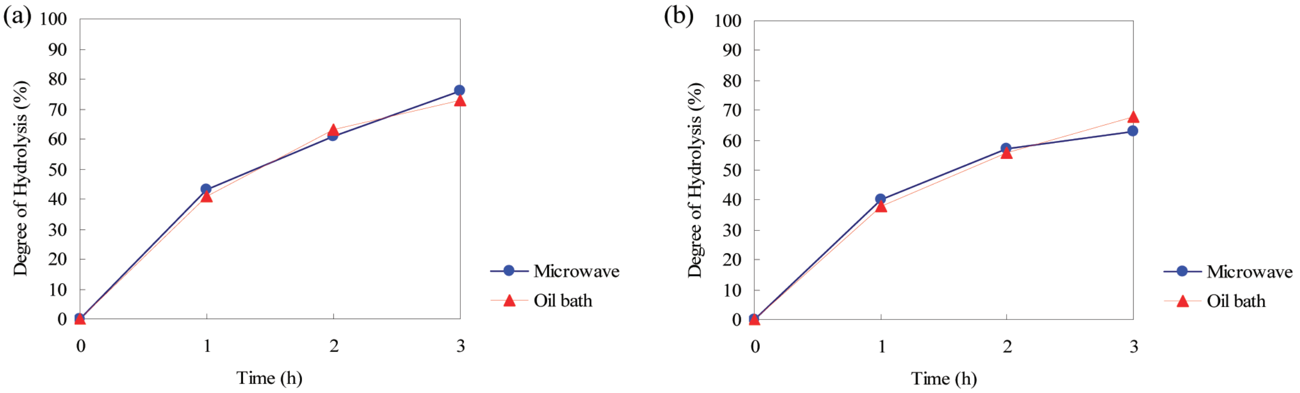


Figure 4. Plot of degree of hydrolysis versus time for hydrolysis of poly(β-alanine) using aqueous NaOH solution (a) or using aqueous KOH solution (b) at 100 °C.

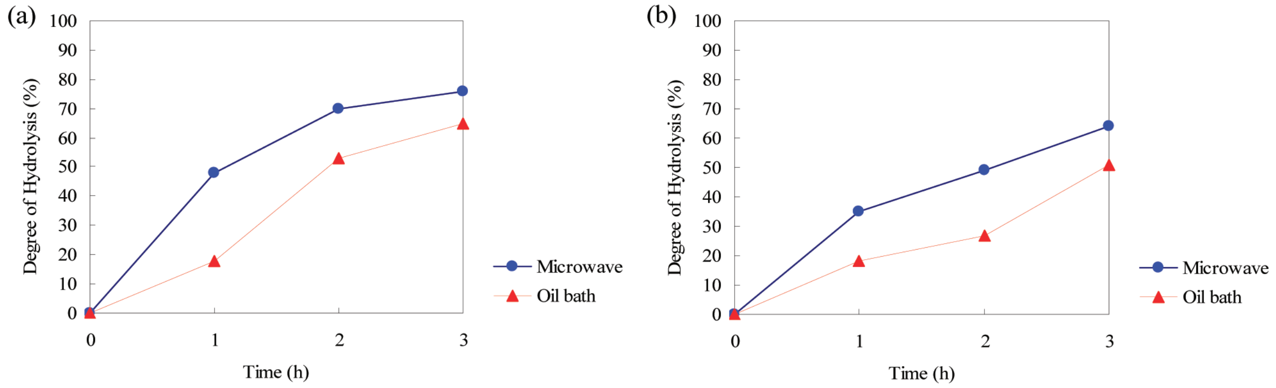
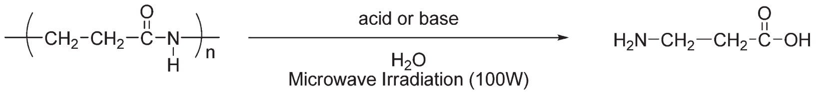


Figure 5. Plot of degree of hydrolysis versus time for hydrolysis of poly(β-alanine) using aqueous HCl solution (a) or using aqueous H_2SO_4 solution (b) at 100 °C.

Scheme 2. Hydrolysis of Poly(β-alanine) under Microwave Irradiation



$$\left(-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-\underset{H}{N}-\right)_n \xrightarrow[\text{Microwave Irradiation (100W)}]{\text{acid or base}} H_2N-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-OH$$

degrees of hydrolysis were determined from ^1H NMR spectroscopy, which showed two kinds of methylene signals at δ 2.60−2.80 and δ 2.33 ppm, as is clearly shown by the relative intensity of these peaks. The degree of hydrolysis reached 62−68% by treatment with a 6 N NaOH aqueous solution at 100 °C for 1−3 h under microwave irradiation. In the case of conventional oil bath heating (100 °C, 1−3 h), in which a solution of poly(β-alanine) with 6 N NaOH aqueous solution was stirred at 100 °C for 1−3 h in an oil bath, the degree of hydrolysis was found to be 60−71%. Figure 4 shows the plot of degree of hydrolysis versus time for hydrolysis of poly(β-alanine) under 6 N NaOH and 6 N KOH aqueous solution conditions. In Figure 4, the differences in the degrees of hydrolysis between microwave irradiation and oil bath heating were not recognizable. In the case of acidic conditions, the differences in the degrees of hydrolysis between microwave irradiation and oil bath heating were recognizable (Figure 5). In the case of 6 N HCl aqueous solution, when compared with oil bath heating, the degrees of hydrolysis of polymer became 11−30% higher by using microwave irradiation. When the hydrolysis of poly(β-alanine) was carried out with 6 N H_2SO_4 aqueous solution, compared with oil bath heating, the degrees of hydrolysis of polymer became 13−22% higher by using microwave irradiation.

We compared the hydrolysis behavior of *N*-methylpropionamide as the low-molecular-weight amide compound with the hydrolysis behavior of poly(β-alanine). An aqueous solution of *N*-methylpropionamide with a base or acid was 100 W microwave irradiated at 50 °C for 1−3 h in the temperature control mode. The degree of hydrolysis reached 43−76% by treatment with a 6 N NaOH aqueous solution at 50 °C for 1−3 h under microwave irradiation. In the case of conventional oil bath heating, in which a solution of *N*-methylpropionamide with 6 N NaOH aqueous solution was stirred at 50 °C for 1−3 h by an oil bath, the degree of hydrolysis was found to be 41−73%. Figure 6 shows the plot of degree of hydrolysis versus time for hydrolysis of *N*-methylpropionamide under 6 N NaOH and 6 N KOH aqueous solution conditions. In Figure 6, the differences in the degrees of hydrolysis between microwave irradiation and oil bath heating were also not recognized. In the case of acidic conditions, the differences in the degrees of hydrolysis between microwave irradiation and oil bath heating were recognized (Figure 7). In the case of 6 N HCl aqueous solution, when compared with oil bath heating, the degree of hydrolysis of *N*-methylpropionamide became 17−32% higher by treatment with a 6 N HCl aqueous solution at 100 °C for 1−3 h under microwave irradiation. When the hydrolysis of *N*-methylpropionamide was carried out with 6 N H_2SO_4 aqueous solution, as compared with oil bath heating, the degree of hydrolysis of the polymer became 16−24% higher by treatment with a 6 N H_2SO_4 aqueous solution

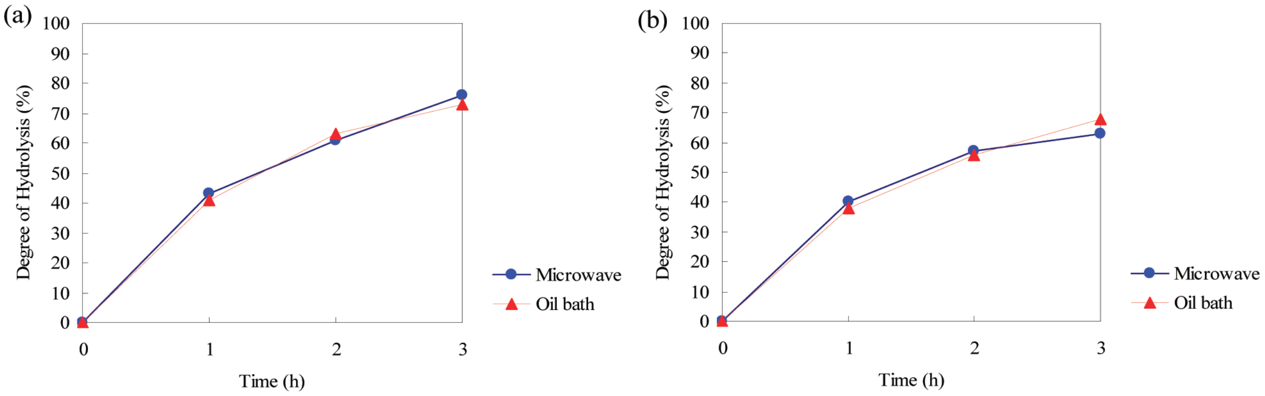


Figure 6. Plot of degree of hydrolysis versus time for hydrolysis of *N*-methylpropionamide using aqueous NaOH solution (a) or using aqueous KOH solution (b) at 50 °C.

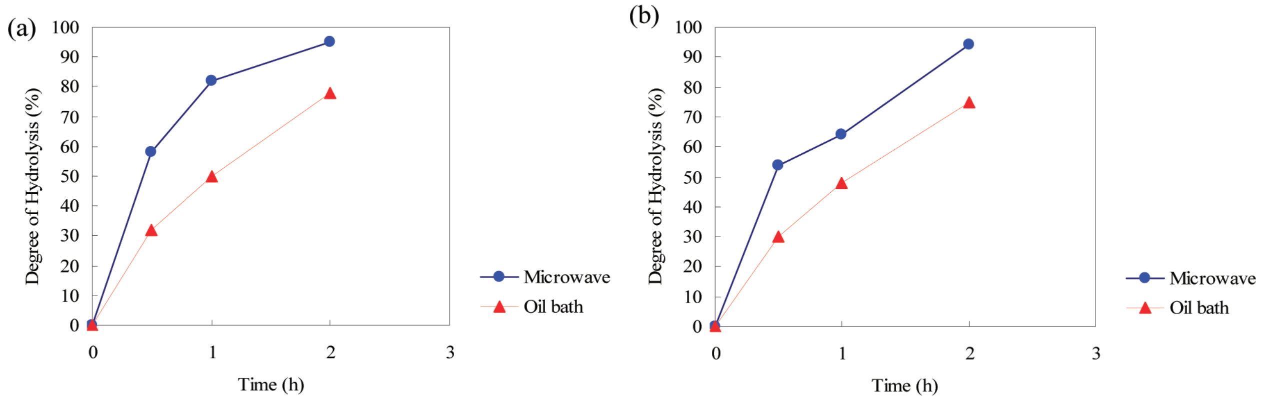
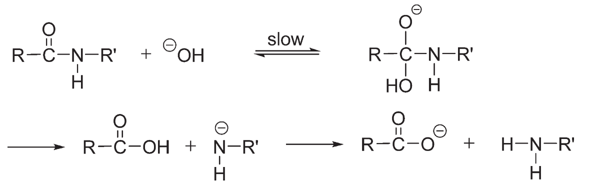
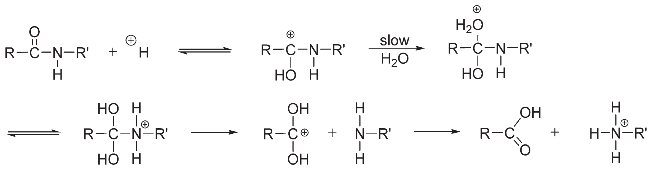


Figure 7. Plot of degree of hydrolysis versus time for hydrolysis of *N*-methylpropionamide using aqueous HCl solution (a) or using aqueous H_2SO_4 solution (b) at 100 °C.

Scheme 3. Hydrolysis Mechanism of Amide Compounds under Basic Conditions



Scheme 4. Hydrolysis Mechanism of Amide Compounds under Acidic Conditions



at 100 °C for 1−3 h under microwave irradiation. From these results, the hydrolytic behavior of a low-molecular-weight amide compound seems to resemble the hydrolytic behavior of poly(β-alanine). That is, there were no differences in the degree of hydrolysis between microwave irradiation and oil bath heating in basic conditions. In contrast with hydrolysis under basic conditions, the difference in the degree of hydrolysis between microwave irradiation and oil bath heating was recognizable in acidic conditions.

Generally, polar and ionic compounds are efficiently heated by microwave irradiation. It is known that the hydrolysis of amide compounds under basic conditions proceed as shown in Scheme 3.[24] In this hydrolysis reaction, the hydroxide anion attacks to the amide in a rate-determining step.[24b] On the other hand, the hydrolysis mechanism of the amide in acidic conditions is less clear, even though it is known that amide is primarily protonated on the oxygen atom of amide. The second step of the reaction is a rate-determining step in acidic conditions (Scheme 4).[25] These reports suggest that a charge was slowly generated on the main chain of the polymer under basic conditions and that a charge was rapidly generated on the main chain of the polymer under acidic conditions. Since a charge was not rapidly generated on the main chain of the polymer under basic conditions, a difference could not be confirmed in the degree of hydrolysis between microwave irradiation and conventional oil bath heating. In contrast to basic conditions, since a charge which was generated on the main chain of the polymer might be heated efficiently under acidic conditions, the hydrolysis of amide might proceed more efficiently. This phenomenon might be due to a nonthermal microwave effect.

Conclusion

The polymerization of acrylamide was carried out using *t*-BuOK as an initiator in DMF under microwave irradiation. As a result, poly(β-alanine) was obtained within a short time (180 s) in a good yield (96%). Compared with conventional oil bath heating, the microwave-assisted polymerization reaction shortened the reaction time to about 1/30. With 100 W, 2.45 GHz microwave irradiation, the formation of polymer was accelerated. Furthermore, the hydrolysis of poly(β-alanine) was carried out using acids or bases under microwave irradiation. Under basic conditions, a difference in the degree of hydrolysis between microwave irradiation and oil bath heating was not recognizable.

However, under acidic conditions, a difference in the degree of hydrolysis between microwave irradiation and oil bath heating was recognizable. In other words, microwave-assisted hydrolysis of poly(β-alanine) clearly proceeded efficiently under acidic conditions. We have demonstrated the basic concepts of chemical recycling for poly(β-alanine) as polyamides. In the future, chemical recycling of polyamides may become possible by the microwave-assisted polymerization-degradation system.

Supporting Information Available: Detailed results of hydrolysis (Tables S1−S4). This material is available free of charge via the Internet at http://pubs.acs.org.

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