

A Novel Synthetic Procedure of Vinylacetamide and Its Free Radical Polymerization

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Synopsis

The pyrolysis of *N*-(α -methoxyethyl)acetamide, which was obtained by one-step reaction of acetamide, acetaldehyde, and methanol, gave *N*-vinylacetamide (NVA) in a good yield. The polymerizability and copolymerizability of NVA were studied. Free radical polymerization was carried out in the presence of radical initiator or by γ -ray irradiation. The monomer reactivity ratios of NVA were estimated in the copolymerization with acrylamide, vinyl acetate, and methyl methacrylate. The solvents were found to influence the monomer reactivity ratio. NVA showed a typical copolymerizability as nonconjugated vinyl monomer, and Q and e values were obtained in DMF as 0.16 and -1.57 , respectively.

INTRODUCTION

In recent years, water soluble monomers and polymers have acquired a great importance as rather biomaterial than chemical modifier. Among them *N*-vinylacetamide (NVA) and its polymer are not only soluble in both water and organic solvents, but important as a precursor to poly(vinylamine). After NVA was first synthesized,¹ Dawson et al.² and Stackman et al.³ developed the synthetic procedure and then polymerized it. However, we can find only few investigations on the further developing synthetic route and the polymerization of NVA and the application of poly(NVA) to functional polymers.

Poly(vinylamine), which is an important and the simplest polycationic water soluble functional polymer, is usually derived from poly(*N*-vinyl-*tert*-butylcarbamate),⁴ poly(*N*-vinylphthalimide),⁵ poly(acrylic acid),⁶ or poly(acrylamide).⁷ When poly(vinylamine) is derived from poly(NVA) by amide hydrolysis, various functional polymers such as poly(vinylamine) graft, poly(vinylamine) block, and partially amino group substituted copolymer can be expected to commonly synthesize. When NVA becomes a commercially available monomer and then both its polymerizability and copolymerizability are clarified, it must be easy to design and synthesize new functional polymers consisting of NVA or vinylamine.

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In this paper, we report the new synthetic route to NVA, which can be applicable to the industrial scale, and the free radical polymerization and copolymerization of it.

EXPERIMENTAL

Materials

The solvents were purified in the usual way prior to use. Commercial styrene, methyl methacrylate, and vinyl acetate were distilled *in vacuo*. Benzoylperoxide (BPO) was precipitated in methanol after dissolving in chloroform, and α,α' -azobisisobutyronitrile (AIBN) was recrystallized from ethanol. Reagent grade acrylamide, potassium persulfate (KPS), 2,2-azobis(*N,N*-dimethyleneisobutyramidine)dihydro-chloride (VA-044: Wako Pure Chemical Ind. Ltd.), and 2,2'-azobis(*N,N'*-dimethyleneisobutyramidine) (VA-061: Wako Pure Chemical Ind. Ltd.) were used without further purification.

N-(α -Methoxyethyl)acetamide (MEA)

A 1 L three-neck flask equipped with a thermometer, a dry-ice condenser and a dropping funnel was charged with 118 g (2 mol) of acetamide, 640 g (20 mol) of methanol and 16.4 g of conc. sulfuric acid. With stirring, 880 g (20 mol) of acetaldehyde was added sequentially and the reaction vessel was heated to reflux for 1 h. After neutralizing the reaction mixture, the unreacted acetaldehyde and methanol were evaporated off. The condensed mixture was extracted with chloroform and water. The aqueous layer was extracted with chloroform three times. The organic layer was combined, evaporated, and distilled (75°C/1.8 mm Hg). In all, 196 g of MEA was obtained. The yield was 83.7% based on acetamide.

N-Vinylacetamide

A 50 mL three-neck flask equipped with a nitrogen inlet and a dropping funnel was connected with a quartz 40 \times 2 cm pyrolysis tube. The tube was filled with a quartz ring. And another side of the tube was connected with two traps. The first trap was immersed in ice/water and second trap was in dry-ice/ethanol. The tube was heated to 550°C with an electric furnace, and the internal pressure was reduced to 5–10 mm Hg. Then the flask was immersed in an oil bath and heated to 150°C. Nitrogen flow was 10 mL/min and 117.0 g of MEA was dropped to the flask at a rate of 1 mL/min. The condensate of the two traps was combined. Distillation at 95–97°C/10 mm Hg gave 76.9 g (90.5%) of the product (colorless cubes, mp 53–54°C (lit.² mp 54–55°C).

Polymerization

Solution polymerization was carried out at 60°C in a sealed tube under shaking in an incubator. Monomer reactivity ratios, r_1 and r_2 values, were estimated from Fineman–Ross plots based on the copolymer composition determined by NMR analysis.

Radiation-induced polymerization was carried out in a sealed tube in a crystalline or solution condition by irradiating with γ -ray from a ^{60}Co source, with a dose rate of 3.1×10^3 dose/h. After the polymerization, the contents were washed with ether to remove unreacted monomer and the remaining solids were dissolved in ethanol and poured into excess ether. The isolated polymer was dried *in vacuo*.

Measurements

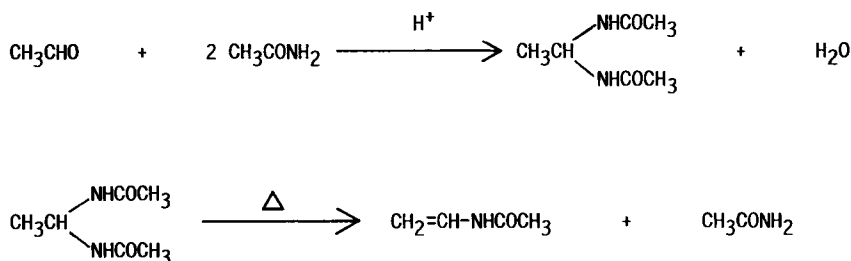
The ^1H -NMR spectra were recorded on JEOL FX-90 (90 MHz) or JEOL GSX-400 (400 MHz) instruments. 3-(Trimethylsilyl)propanesulfonic acid sodium salt (DSS) was used as internal reference in D_2O . The number average molecular weight was measured by vapor pressure osmometry (VPO; Corona Model 117 osmometer) in water at 60°C . Gel permeation chromatographic (GPC) analysis was performed on a Simadzu LC-6A equipped with RI detector (Shodex SE-51) with a Shodex column (B-806, 8×500 mm). Distilled water was used as eluent at flow rate of 1.0 mL/min. Differential scanning calorimetry (DSC) of poly(NVA) was carried out by a Simadzu DSC-50 calorimeter under nitrogen at a $10^\circ\text{C}/\text{min}$ heating rate.

RESULTS AND DISCUSSION

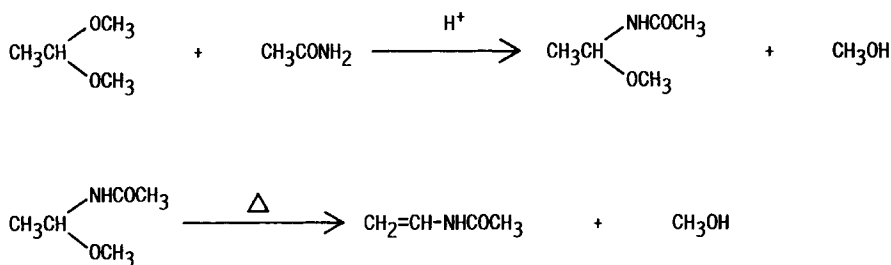
Synthesis of NVA

Dawson synthesized NVA by two step reaction of acetamide and acetaldehyde as shown in Scheme 1. Although this process is simple, it is very difficult to obtain pure NVA. Because substantial amount of acetamide is produced when the pyrolysis of ethylidene bisacetamide, and produced acetamide and NVA have very close boiling point and similar solubility to organic solvents, the separation of the reaction mixture is not accomplished without difficulty.

Stackman showed the process for the synthesis of NVA from dimethyl acetal and acetamide by two step reaction as shown in Scheme 2. This process contains the pyrolysis of *N*-(α -methoxyethyl)acetamide, which is essentially described in a Hoechst patent,⁸ and NVA was obtained in a good yield and pure form. But this process needs very large excess of acetal (20 eq of acetamide). Moreover, acetal is not always so available in a large scale, especially in a manufacturing plant, that the handling and the isolation of acetal are in serious question.

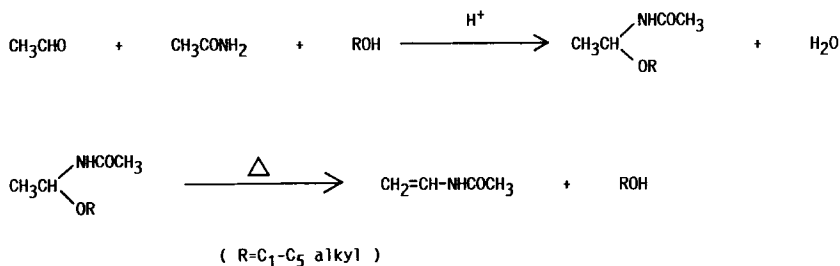


Scheme 1.



Scheme 2.

We found the alternative process of synthesizing the *N*-(α -alkoxyethyl)acetamide by the one step reaction of acetamide, acetaldehyde, and alcohol (Scheme 3). In the present process, the starting materials are very easily available and the reaction is accomplished with easy operation. In comparison with Stackman process, the reaction proceeds at lower temperature. While the reaction of acetal and acetamide proceeds very slowly at room temperature, the "one-step reaction" does smoothly at the same temperature. This fact suggests that the mechanism of the reaction is not via acetal at least at room temperature. The intermediate of the reaction must be hemiacetal [$\text{CH}_3\text{CH}(\text{OH})\text{OR}$] or the adduct of acetaldehyde and acetamide [$\text{CH}_3\text{CH}(\text{OH})\text{NHCOCH}_3$], although these species were too unstable to isolate. The "one-step process" is of advantage in the synthesis of NVA as following points: (1) the intermediate is not needed to isolate; (2) various alcohols such as methanol, ethanol, 1-propanol, 2-propanol, 1-butanol and 1-pentanol are possible to use; (3) in Scheme 2, unreacted dimethyl acetal prevents the precipitation of ethylidene bisacetamide, but in the "one-step process" water generated by the reaction works as a good solvent to prevent the precipitation of ethylidene bisacetamide. Moreover, higher alcohol can be used, and wide variety of etheramides may be easily synthesized. After the reaction mixture achieves equilibrium, it is easily neutralized by alkali. The reaction mixture can be applied to the next reaction step without any purification, but unreacted acetamide remains after the pyrolysis. Therefore, it is preferable to purify the etheramide before the pyrolysis step. When methanol was used as alcohol in the present reaction, MEA was obtained in a high yield (83.7%) by the extraction from the reaction mixture and distillation. If acetamide is not removed from etheramide, the lowering of the purity of NVA



Scheme 3.

obtained by pyrolysis is unavoidable and it is not easy to separate acetamide from NVA. In order to rise up the conversion of acetamide, an excess amount of acetaldehyde and alcohol may be used because the reaction is equilibrium reaction. In the reaction acid catalysis acts effectively, therefore more consideration of both homogeneous and heterogeneous catalyst may give a developed process of NVA synthesis.

Polymerization of NVA

Free radical polymerization of NVA was carried out in various solvents at 60°C in the presence of KPS, VA-044, BPO, or AIBN. Moreover γ -ray irradiation polymerization was performed in solid state or in water or ethanol in the presence or absence of added initiator. Figure 1 shows the time-conversion curves for the polymerization of NVA. The results are summarized in Table I. The resulting polymer, poly(NVA), is colorless, amorphous, and soluble in water, methanol, ethanol, DMSO, DMF, and insoluble in benzene, dioxane, and chloroform. In water, ethanol, and DMF, the polymerization proceeds homogeneously, while in dioxane and benzene resulting polymers precipitate in the course of polymerization. The polymerizability of NVA in both water and organic solvent was fairly good regardless of its solubility, but when peroxides were used as initiator the conversion was extremely low as pointed out by Stackman.³ The NMR spectra of polymerization systems using deuterium solvents show that NVA is reacted with KPS in D_2O to give the hydrolyzates and with BPO in $DMSO-d_6$ to decompose. Consequently, in the polymerization of NVA adequate initiator has to be chosen. The polymerization of NVA proceeded faster in benzene than in ethanol. This may be ascribed that molecular aggregate of NVA by intermolecular hydrogen bond is of advantage in the propagation

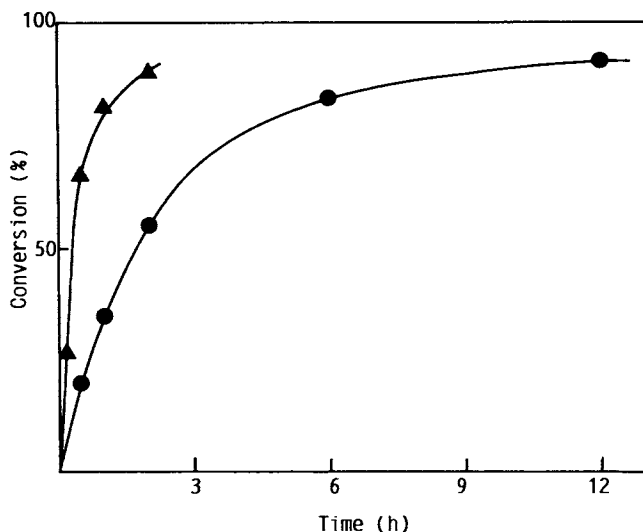


Fig. 1. Time-conversion curves for the polymerization of NVA. Solvent: (●) ethanol, (▲) benzene.

TABLE I
 Polymerization of NVA at 60°C for 12 h^a

Run	Solvent	Initiator	[NVA]/[I]	Yield (%)	\overline{M}_n^b	$[\eta]$ (dL/g)
1	H ₂ O	K ₂ S ₂ O ₈	100	3		
2	H ₂ O	VA-044	100	99		0.64
3	Ethanol	BPO	50	13		
4	Ethanol	AIBN	100	90	12300	0.56
5	Ethanol	AIBN	500	81		0.85
6	Ethanol	AIBN	1000	65		0.94
7	DMF	AIBN	100	80	6600	
8	Dioxane	AIBN	100	88	4900	
9	Benzene	AIBN	100	82	3200	

^a 6 mmol of NVA was used in 3 mL of solvent.

^b Estimated by VPO.

step of the polymerization. From the NMR spectroscopy, actually, when the concentration of NVA increased, the chemical shift of amide proton of it in CDCl₃ shifted to lower field owing to hydrogen bonding formation.

Interestingly, solid-state polymerization of NVA took place as well as in water and ethanol by γ -ray irradiation without any added radical initiator. GPC analysis of the polymerization system was performed and the results are shown in Figure 2. The molecular weight of the polymer obtained in solid state by γ -ray irradiation was relatively high and increased with the elapse of time, while this tendency was not observed in the solution polymerization of NVA. Table II shows the results and the stereoregularity of poly(NVA). The 400 MHz NMR spectra of poly(NVA) (run No. 4) in D₂O and poly(vinylamine) derived from poly(NVA) by acid hydrolysis^{9,10} are shown in Figure 3. Poly(NVA) was completely converted to poly(vinylamine) and almost no remaining acetamide peak was detected. Three peaks at 1.58, 1.93, and 3.77 ppm obtained in the intensity ratio of 2 : 3 : 1 can be assigned to the protons of methylene, methyl and methyne, respectively (Scheme 4).

Figure 4 shows the 400 MHz ¹H-NMR spectra observed for poly(NVA) obtained by γ -ray irradiation polymerization. The acetamide methyl proton resonance of poly(NVA) consists of three principal signals. The peaks at 1.90, 1.93, and 1.98 ppm can be assigned to the component of the syndiotactic triad (S), heterotactic triad (H), and isotactic triad (I), respectively, according to the literature.^{9,10} Triad tacticity of poly(NVA) was estimated by calculating the areas of the three peaks. It is reported that poly(NVA) has a highly syndiotactic structure⁹ or atactic structure,¹⁰ but the present results shows it has a rather isotactic structure by solid state polymerization, especially at 0°C. It can be assumed that crystal structure of NVA may be suitable for isotactic propagation of poly(NVA), since γ -ray polymerization of NVA in ethanol at 0°C gave the atactic polymer similarly to the polymer obtained with free radical initiator in solution.

The T_g values of both isotactic and atactic poly(NVA) were almost same (174°C) by DSC measurements.

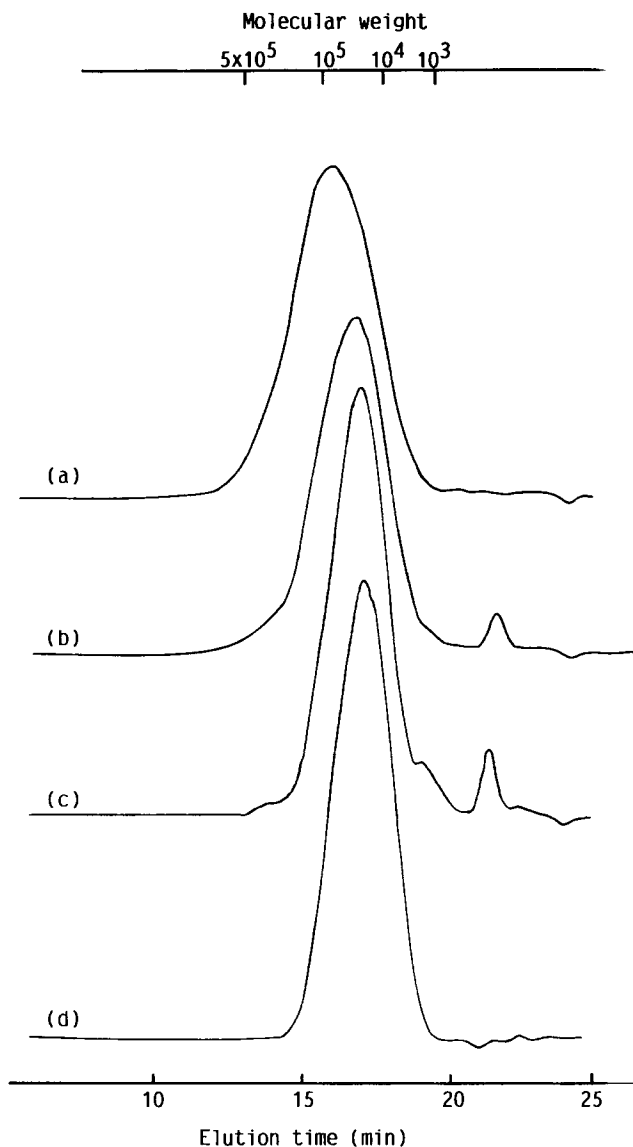


Fig. 2. GPC profiles of poly(NVA)s. The polymers were obtained by γ -ray irradiation at RT for (a) 5 h, (b) 3 h, (c) 1 h, and (d) by free radical polymerization in the presence of AIBN at 60°C for 12 h.

Copolymerization of NVA

Though the free radical copolymerization between NVA and vinyl acetate was reported by Stackman,³ a detailed study on it has not been developed. The copolymerization between NVA (M_1) and a few typical vinyl monomers (M_2) was carried out at 60°C in a variety of solvents in the presence of AIBN as an initiator. The monomer reactivity ratios were estimated from Fineman-Ross plots, and the data are summarized in Table III. For the copolymerization

TABLE II
Radiation-Induced Polymerization of NVA and Stereoregularity of PolyNVA^a

Run	Solvent	Temperature (°C)	Yield (%)	\overline{M}_n^b ($\times 10^{-3}$)	Tacticity (%)		
					I	H	S
10	none	RT	41	800	44	41	15
11	none	0	9		50	40	10
12 ^c	Ethanol	0	46	12.1	27	53	20
13	Ethanol	0	50	12.4	26	54	20
14	H ₂ O	RT	80		29	50	21
4 ^d	Ethanol	60	90	12.3 ^e	25	53	22

^a 4 mmol of NVA was used; time: 5 h; total dose: 1.53×10^4 Gy.

^b Estimated by GPC. Pullulan or poly(ethylene oxide) was used for the molecular weight calibration.

^c 1 mol % of VA-061 was added.

^d See Table I.

^e Estimated by VPO.

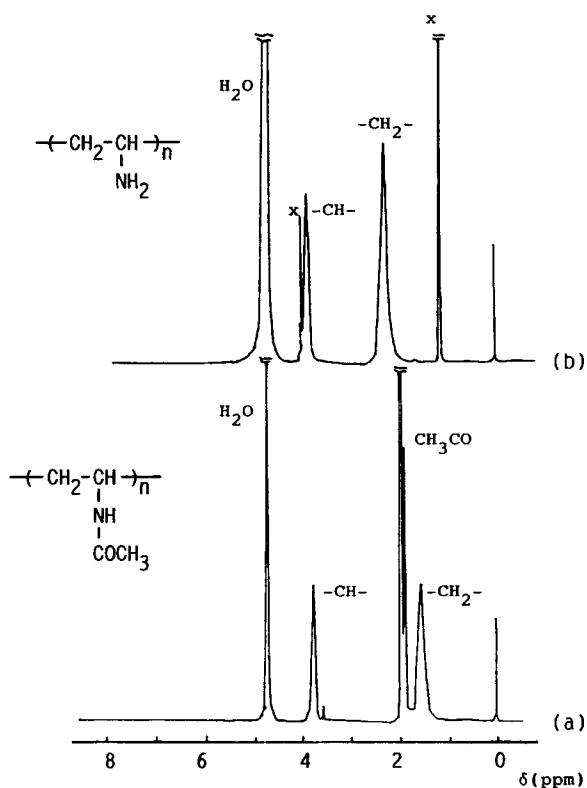
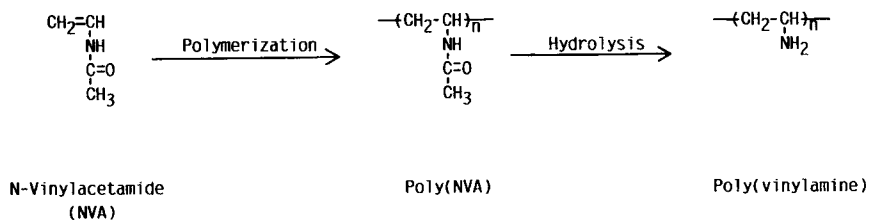


Fig. 3. ¹H-NMR spectra of (a) poly(NVA) and (b) poly(vinylamine) in D₂O.



Scheme 4.

between NVA and vinyl acetate in methanol, r_1 is much larger than r_2 , and the $r_1 r_2$ value is unusually large. The results suggest that the growing radical of NVA more easily propagates to the NVA monomer than to vinylacetate, and the copolymerization tends to proceed for giving block copolymers. The co-

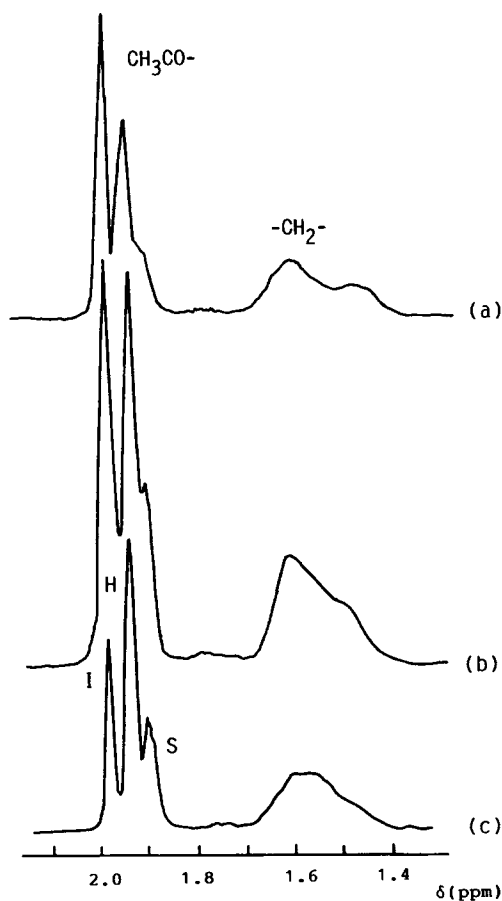


Fig. 4. ^1H -NMR spectra of poly(NVA)s in D_2O . The polymers were obtained by γ -ray irradiation at (a) 0°C (run 11), (b) RT (run 10), and (c) by free radical polymerization in the presence of AIBN at 60°C (run 4).

TABLE III
 Monomer Reactivity Ratio of NVA^a

M ₁	M ₂	Solvent	<i>r</i> ₁	<i>r</i> ₂	<i>r</i> ₁ <i>r</i> ₂
NVA	Acrylamide	Ethanol	0.3	1.4	0.42
NVA	Vinyl acetate	Methanol	5.5	0.6	3.3
NVA	Vinyl acetate	Benzene	21	≈ 0	—
NVA	Methyl methacrylate	Ethanol	0.19	2.65	0.50
NVA	Methyl methacrylate	Benzene	0.71	1.18	0.83
NVA	Methyl methacrylate	DMF	0.01	2.1	0.21

^a Initiator: AIBN; [Total monomer]/[AIBN] = 100.

polymerization of NVA with methyl methacrylate was investigated in order to evaluate *Q* and *e* values of NVA. Poly(methyl methacrylate) and methyl methacrylate-rich copolymers precipitate in ethanol, poly(NVA), and NVA-rich copolymer do in benzene. In DMF the copolymerization proceeds homogeneously. Generally free-radical copolymerization is not so influenced by any solvent, while the present results suggest that solvent influences strongly the copolymerization of NVA as shown in the copolymerization of 2-hydroxyethyl methacrylate,¹¹ acrylamide derivatives,¹² and methacryloyl type derivatives of nucleic acid bases.^{13,14} It can be assumed that the amide group of NVA aggregates intermolecularly by hydrogen bonding interaction and then the reactivity of monomers changes markedly. NVA has a high monomer reactivity ratio in benzene, which suggests that NVA aggregates in this solvent by hydrogen bonding interaction as similarly as 2-hydroxyethyl methacrylate¹¹ and acrylamide derivatives.¹² Ethanol and DMF, in which poly(NVA) dissolves, cause the dissociation of the aggregation of NVA owing to the strong interaction between NVA and solvents. It has been definitely shown by the copolymerization of methacryloyl type monomers containing nucleic acid bases in various solvents that hydrogen bonding interaction of monomers plays a role in the propagation step,¹⁴ which supports the present explanation.

Evaluation of *r*₁ and *r*₂ from the *Q*-*e* scheme might be meaningless in this system.¹¹ However, when the solvent interacts both monomers strongly, considerably reliable values can be obtained. Both poly(NVA) and poly(methyl methacrylate) dissolve in DMF, which suggests that strong interactions exist between monomers and solvent. Consequently, the *Q* and *e* values were estimated from the data obtained in DMF as *Q* = 0.16 and *e* = -1.57 (for methyl methacrylate, *Q* = 0.74 and *e* = 0.40).¹⁵ These values are quite similar to those of *N*-vinylpyrrolidone (*Q* = 0.14 and *e* = -1.14).¹⁵

In conclusion, NVA is classified as nonconjugated type vinyl monomers similarly as vinylpyrrolidone or vinyl acetate and possesses high radical polymerizability, though the hydrolysis of amide group has to be cared in polymerization system. The study of functional polymers derived from NVA will be reported in a future study.

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