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Synthesis of Novel Polymers Based on High Reactivity of Activated Isocyanates

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Chapter 1

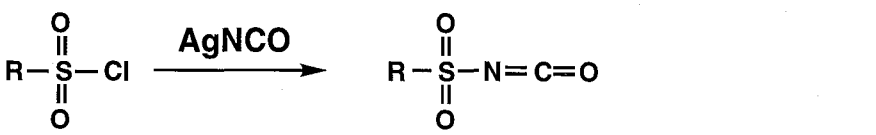
General Introduction

Chemistry of Activated Isocyanates

The chemistry of isocyanates dates back over one hundred years. The first members of this class of compounds were synthesized by Wurtz in 1848, and many of its reactions, especially nucleophilic substitution reactions, dimerization, and trimerization were investigated extensively by Wurtz and Hofmann in the last century.[1] A causal combination of events, starting with the synthesis of isocyanates from amines and phosgene, discovery of polyamide by Bayer successful polyaddition of diisocyanates with diol led to the enormous interest in isocyanates today.[2] That is, in the wake of Bayer's discovery, the chemistry of isocyanates has been thoroughly investigated.

Novel types of activated isocyanates having electron-withdrawing groups on the α-position of isocyanate moieties, and their specific reactions have been discovered since 1903.

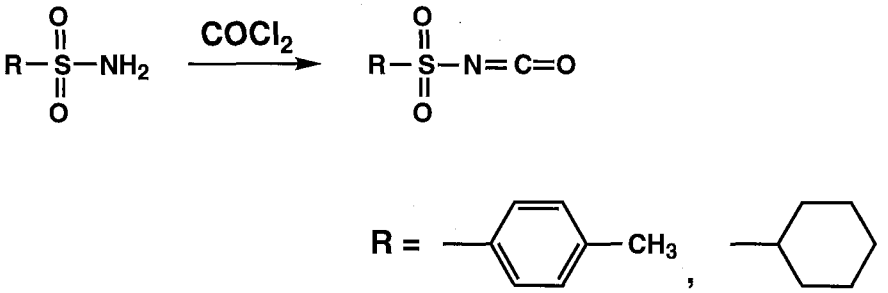
Sulfonyl isocyanates having a sulfonyl group adjacent to the isocyanate moiety (RSO_2NCO, where R represents halogen, alkyl, or aryl groups) were first obtained by Billeter in 1903. The classical method of synthesis involves the reaction of sulfonyl chlorides with silver cyanate, by which methane as well as benzenesulfonyl isocyanates were obtained in low yields (5-38%) (Scheme 1).[3]



$R = CH_3, C_6H_5$

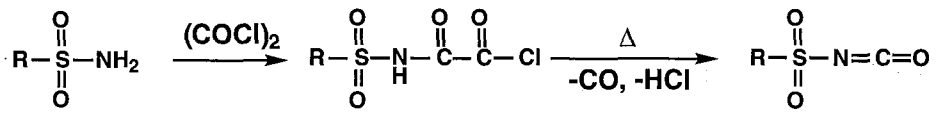
Scheme 1

Similar to ordinary isocyanates, sulfonyl isocyanates can be prepared by using phosgene. In 1951, Krzikalla reported the high temperature reaction of *p*-toluenesulfonamide with phosgene leading directly to *p*-toluenesulfonyl isocyanate in yields of more than 80%. [4] However, King repeated the Krzikalla's procedure, and claimed on the reported yield to be doubtful. [5] Cyclohexanesulfonyl isocyanate has been also synthesized from phosgene with cyclohexanesulfonamide, although neither yield nor experimental details was clarified (Scheme 2). [6]

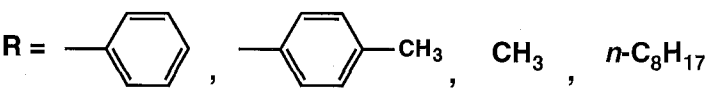


Scheme 2

In 1964, Franz *et al.* reported the reaction of *p*-toluenesufonamide with oxalyl chloride to obtain *p*-toluenesulfonyl isocyanate, [7] in which an initially generated oxamoyl chloride (**I**) undertakes pyrolysis to afford *p*-toluenesulfonyl isocyanate (Scheme 3).

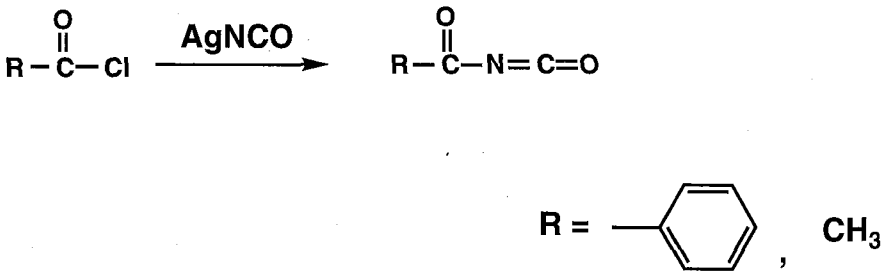


I

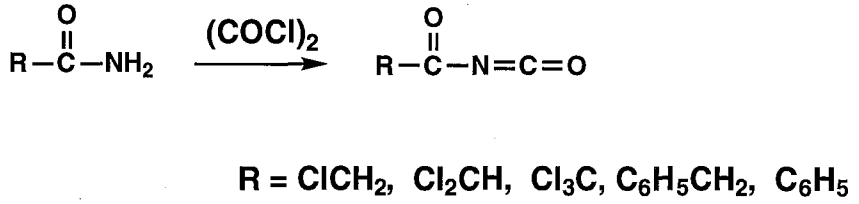


Scheme 3

Acyl isocyanates having the isocyanate group attached to carbonyl groups (RCONCO, where R = Cl, R_2N, RS, RO, or ArO) followed similar history of synthesis. In 1903, they were first prepared by Billeter by the reaction of acyl chlorides with silver cyanate (Scheme 4).[8] In the case of acyl isocyanates, however, the synthetic method using phosgene has not been reported so far. In 1963, Speziale *et al.* reported that the reaction of amides with oxalyl chloride yields acyl isocyanates (Scheme 5).[9]



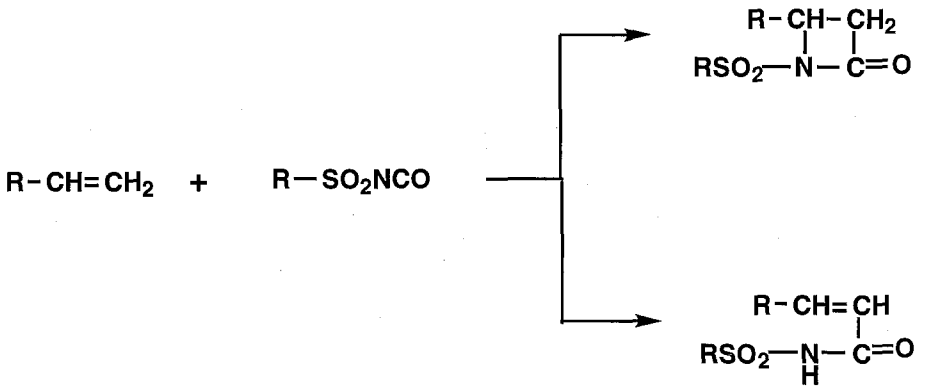
Scheme 4



Scheme 5

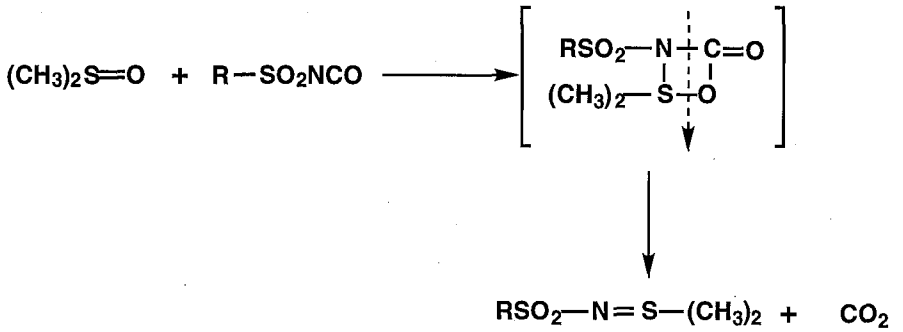
The reaction of activated isocyanates with nucleophiles (i.e., alcohol, thiol, amine, amide, and olefin) gives the corresponding adducts having active hydrogens.[10] Especially, the specific reactivities of activated isocyanates can be seen in the reaction with weak nucleophiles. Chloro- and fluorosulfonyl isocyanates react with a number of olefins to form 1,2-dipolar addition products. Generally, the reaction gives the cyclic and/or

straightchain isomers as shown in Scheme 6.[11]



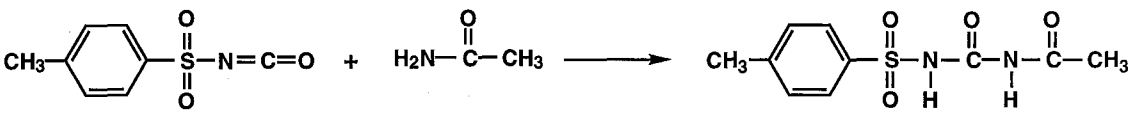
Scheme 6

Dimethyl sulfoxide reacts with *p*-toluenesulfonyl isocyanate to form a sulfilimine derivative by releasing carbon dioxide (Scheme 7).[5]



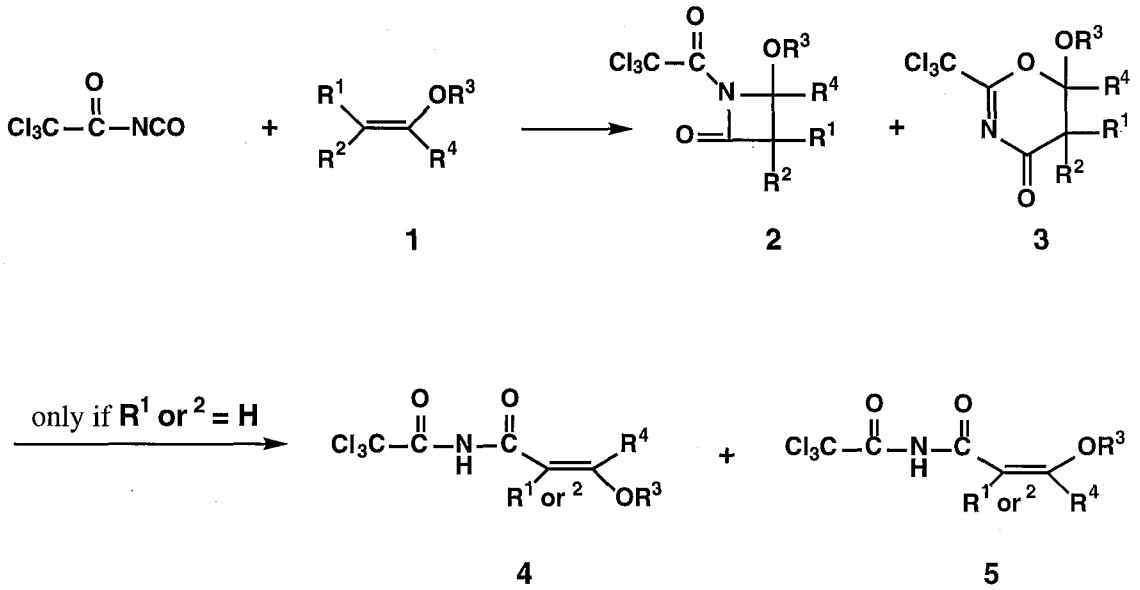
Scheme 7

The reaction of *p*-toluenesulfonyl isocyanate with amides such as acetamide offers products of simple addition, *N*-*p*-toluenesulfonyl-*N'*-acylurea, in high yields (Scheme 8).[5] However, the reaction of *p*-toluenesulfonyl isocyanate with *N*-alkyl amides such as *N*-isobutylacetamide has been reported not to be clean and the yield of the adducts is generally low.[5]



Scheme 8

The reaction of acyl isocyanate such as trichloroacetyl isocyanate with vinyl ethers gives 1:1 adducts, where 3-alkoxy-*N*-(trichloroacetyl)acrylamides (**4** and **5**) were obtained as major components. The reaction is believed to proceed *via* four- and six-membered cyclic intermediates (**2** and **3**), because both of which could be observed by spectroscopic methods. The intermediates (**2** and **3**) subsequently isomerize to linear products (**4** and **5**) (Scheme 9).[12)]



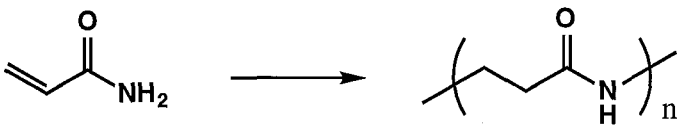
Scheme 9

Owing to the high reactivities of activated isocyanates, it might be possible to modify conventional vinyl monomers having less reactive functional groups such as an amide group, by which it might be possible to synthesize new monomers and consequently new polymers having interesting characters. The reaction of activated isocyanates with monomers

possessing weak nucleophilic centers such as acrylamides will give rise the corresponding adducts as novel monomers having active hydrogens. Since some vinyl monomers having active hydrogens are known to undertake the hydrogen-transfer polymerization, these monomers might reveal interesting polymerization behavior under the anionic conditions.

Hydrogen-Transfer Polymerization

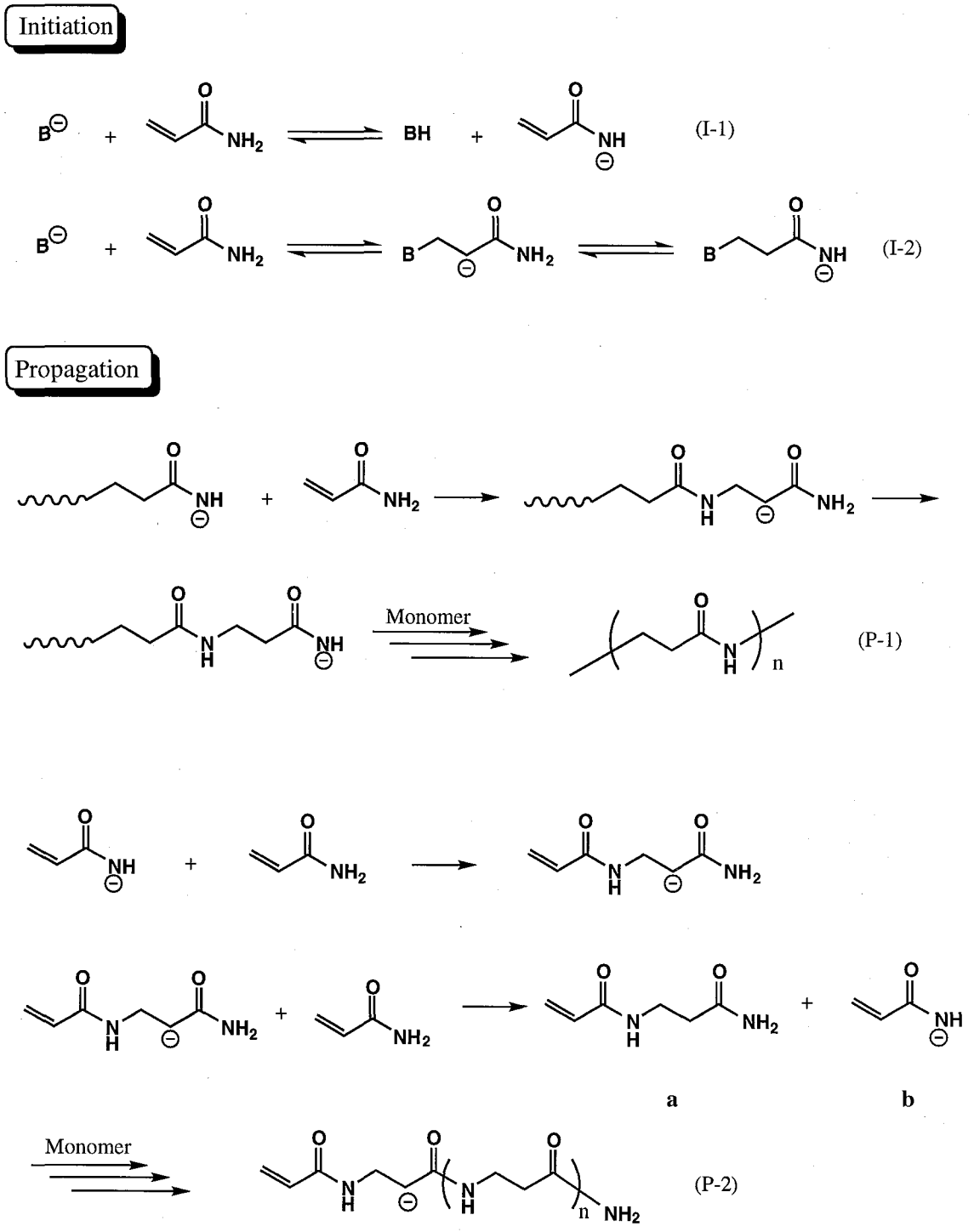
Generally, vinyl monomers having active hydrogens such as acrylamide are known to undertake the hydrogen-transfer polymerization under basic conditions to give rise polymers possessing functional groups in the main chain. The first and most investigated hydrogen-transfer polymerization by anionic initiator is that of acrylamide to give poly(β-alanine) (Scheme 10).[13]



Scheme 10

This system was first patented in 1954 by Matlack and published in 1957 by Breslow *et al.*,[14, 15] in which they described that poly(β-alanine) was obtained when a solution of sodium *t*-butoxide in *t*-butyl alcohol and acrylamide were heated in the presence of a radical-polymerization inhibitor. The structure of the polymer was successfully confirmed by hydrolysis with sulfuric acid to yield β-alanine. Although the polymerization can be regarded to proceed by the conjugate addition of the

N-anions toward acrylamide, two points in the polymerization mechanism are still remained obscure.



Scheme 11

An initiation process have been proposed two possible paths, that is, either the deprotonation (I-1) or the nucleophilic attack (I-2) of the initiator. Breslow *et al.* supported the former path (I-1) for the initiation mechanism, because they could also identify an unsaturated dimer in the reaction mixture and because they could detect a terminal olefin structure in the polymer.[15] On the other hand, Ogata supported the latter mechanism (I-2) on the basis of the IR spectrum of the polymer in which they attributed a peak for the ether linkage.[16]

Two possible mechanisms are also proposed for the propagation by taking intra- (P-1) and inter-molecular (P-2) proton abstractions into consideration, although both of the mechanisms have not been supported by the sufficient evidence (Scheme 11).

Similar to acrylamide, *N*-substituted acrylamides such as *N*-methylacrylamide, *N*-cyclohexylacrylamide, *N*-phenylacrylamide etc., give polymers by hydrogen-transfer mechanism under the anionic conditions.[17, 18]

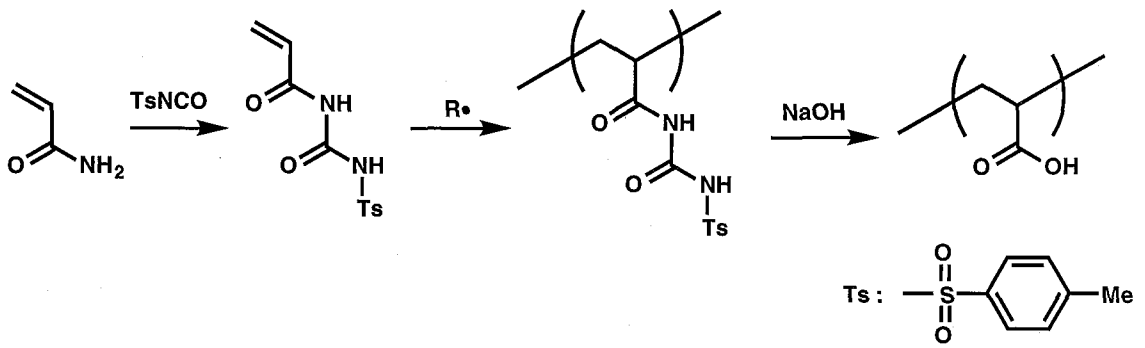
Monomer having α- and β-substituted acrylamide structures also undertake the hydrogen-transfer polymerization.[15,19] Generally the polymerizations of these monomers are slower and the molecular-weight of resulting polymer are much lower than the case of acrylamide, which are explained by the steric effect.

As mentioned above, the hydrogen-transfer polymerization is a promising technique that can introduce functional groups into the main chain of polymers. Therefore, by designing monomers with both appropriate functional groups and active hydrogens, it might be possible to construct novel polymers *via* the hydrogen-transfer process.

Survey of This Thesis

On the basis of the research background as mentioned above, this thesis describes syntheses and polymerization of novel monomers prepared with activated isocyanates.

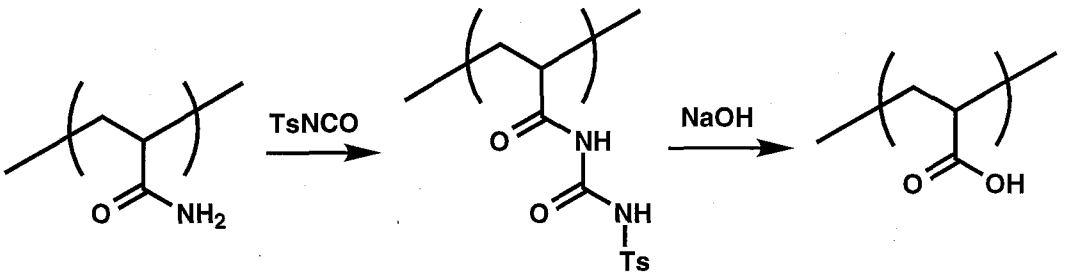
In Chapter 2, the synthesis and the radical polymerization of a monomer having a sulfonylurea moiety (i.e., *N*-acryloyl-*N'*-*p*-toluenesulfonylurea) derived from *p*-toluenesulfonyl isocyanate and acrylamide are described. The radical polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea, prepared easily by the reaction of *p*-toluenesulfonyl isocyanate with acrylamide, was carried out by using AIBN as an initiator to give a polymer having sulfonylurea moieties in a good yield. Copolymerization parameters of the monomer were evaluated by the copolymerization with MMA. Additionally, the polymer was found to undertake hydrolysis in 1 *M* NaOH aqueous solution at room temperature to give poly(acrylic acid) (Scheme 12).



Scheme 12

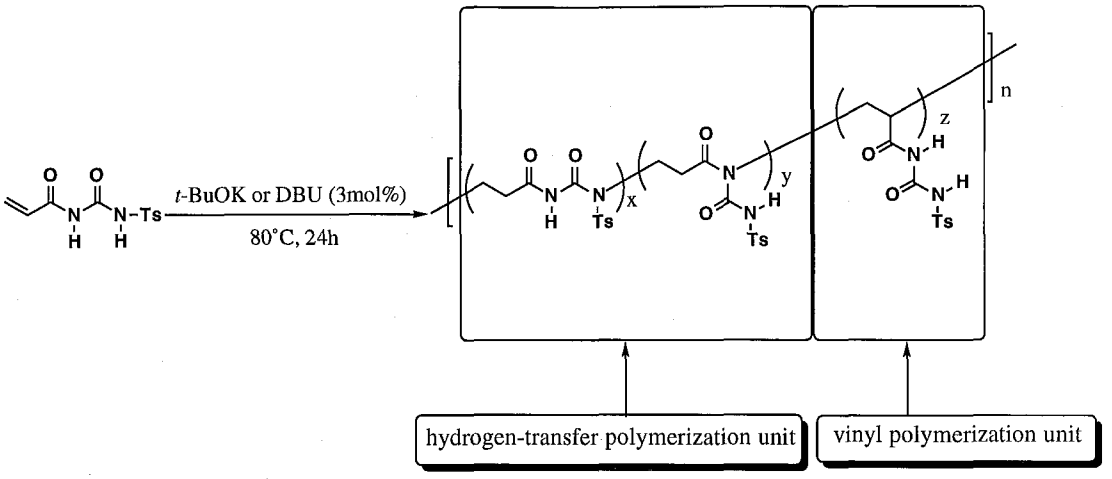
In Chapter 3, the reaction of *p*-toluenesulfonyl isocyanate with polymers having amide moieties and hydrolysis of the obtained polymer are described. The structural modification of polymers having amide

moieties was carried out with *p*-toluenesulfonyl isocyanate. For example, poly(acrylamide) was refluxed with an excess amount of *p*-toluenesulfonyl isocyanate in THF for 50 h to obtain a structurally modified polymer in 76% yield whose sulfonylurea functionality was 100%. The resulting polymer was subjected to hydrolysis in 1*M* NaOH solution at 50°C, by which 90% of the sulfonylurea moieties in the side chains was converted to the carboxylic acid group (Scheme 13).



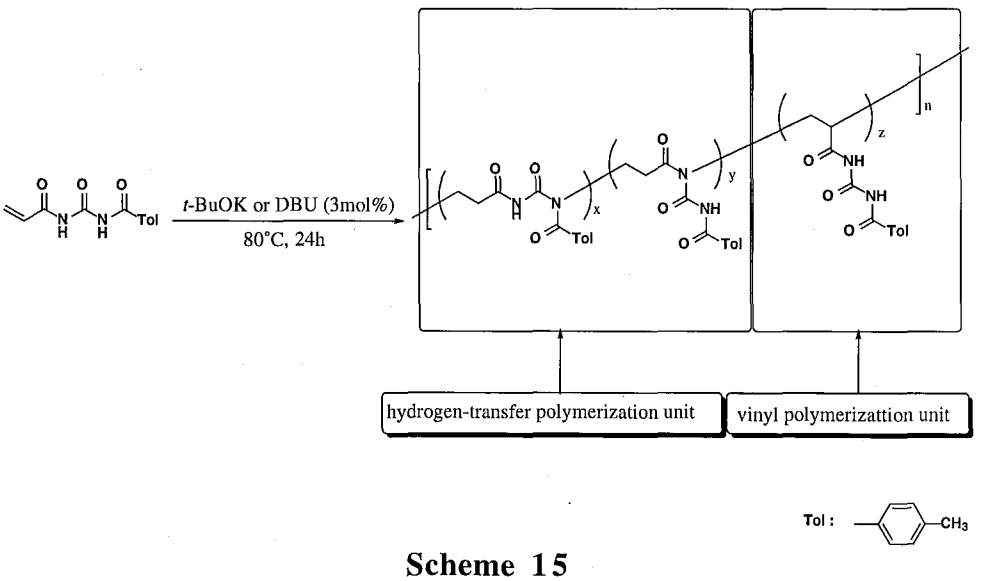
Scheme 13

In Chapter 4, the hydrogen-transfer polymerization of monomers having sulfonylacylurea moieties derived from *p*-toluenesulfonyl isocyanate and acrylamide derivatives is described. The hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea was carried out at 80°C for 24 h using *t*-BuOK or 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), (3 mol%) as an initiator. In all cases, polymers were obtained in moderate yields, whose structures were dependent upon the polymerization conditions. That is, the polymer prepared by *t*-BuOK in polar solvents such as DMF and DMSO was composed of the hydrogen-transfer polymerization unit selectively, while that by *t*-BuOK in less polar solvents such as toluene or by DBU was composed of both the hydrogen-transfer and the vinyl polymerization units (Scheme 14).



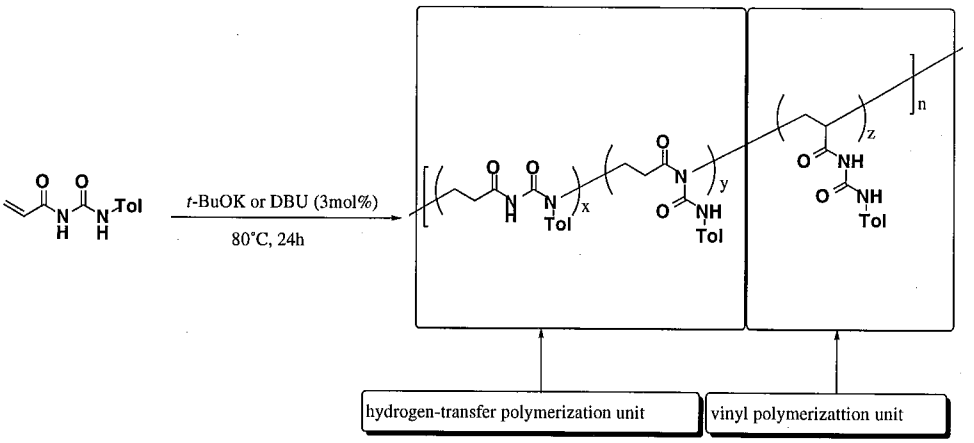
Scheme 14

Chapter 5 deals with the hydrogen-transfer polymerization of monomers having diacylurea moieties derived from 4-methylbenzoyl isocyanate and acrylamide derivatives. The hydrogen-transfer polymerization of *N*-acryloyl-*N'*-(4-methylbenzoyl)urea was carried out at 80°C for 24 h in DMF, DMSO, acetonitrile, or toluene by *t*-BuOK or DBU (3 mol%) as an initiator to obtain a polymer in a good yield. The structure of the obtained polymer was dependent upon the initiator used, in which *t*-BuOK selectively conducted the hydrogen-transfer polymerization, while DBU partially induced the vinyl polymerization (16-20%) (Scheme 15).



Scheme 15

In Chapter 6, the hydrogen-transfer polymerization of monomers having acylurea moieties derived from tolyl isocyanate and acrylamide derivatives is described. The hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-tolylurea was carried out at 80°C in DMF, DMSO, acetonitrile, or toluene for 24 h using *t*-BuOK or DBU (3 mol%) as an initiator to obtain a polymer in a moderate yield. The resulting polymer was composed of the hydrogen-transfer polymerization unit when *t*-BuOK was used as an initiator. In the case of DBU, polymer was composed of both the hydrogen-transfer and vinyl polymerization unit (Scheme 16).



Scheme 16

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Chapter 2

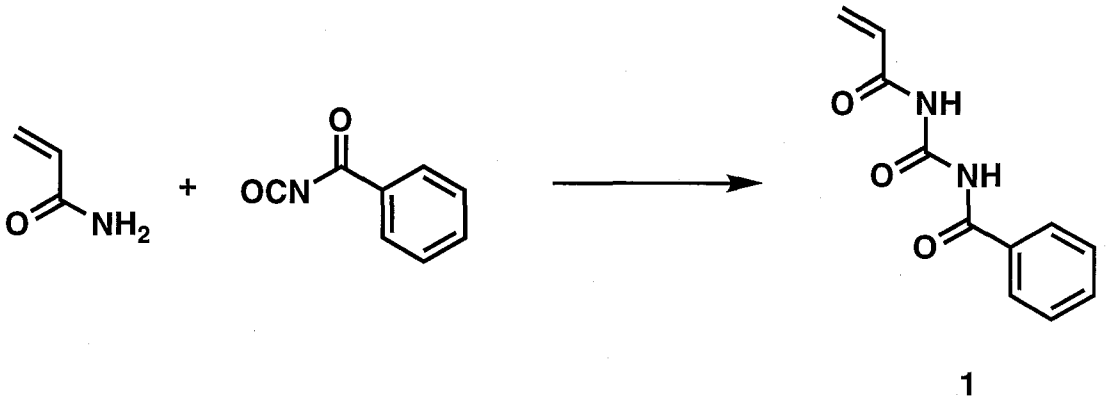
Synthesis and Radical Polymerization of Monomer Having Acylsulfonylurea Moiety Derived from *p*-Toluenesulfonyl Isocyanate and Acrylamide and Hydrolytic Character of the Obtained Polymer

Abstract

The radical polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**2**), prepared easily by the reaction of *p*-toluenesulfonyl isocyanate with acrylamide, was carried out in DMF, DMSO, or NMP at 60°C by use of AIBN as an initiator to give a polymer **3** in a good yield. Copolymerization parameters of **2** were evaluated by the copolymerization with MMA. Polymer **3** was readily hydrolyzed in 1 *M* NaOH aqueous solution at room temperature to give poly(acrylic acid).

2.1 Introduction

Isocyanates bearing electron-withdrawing substituents (i.e., activated isocyanates) are known to reveal high reactivities toward active hydrogens. [1] Modifications of monomers carrying active hydrogens with activated isocyanates may provide new monomers, and consequently, new polymers having unique functions. Recently, Kanamaru *et al.* reported the radical polymerization of *N*-acryloyl-*N'*-benzoylurea (**1**) which could be prepared by the reaction of acrylamide with benzoyl isocyanate (Scheme 1).[2] Monomer **1** revealed a good radical polymerizability and the resulting polymer was found to have an interesting hydrogen bonding character.



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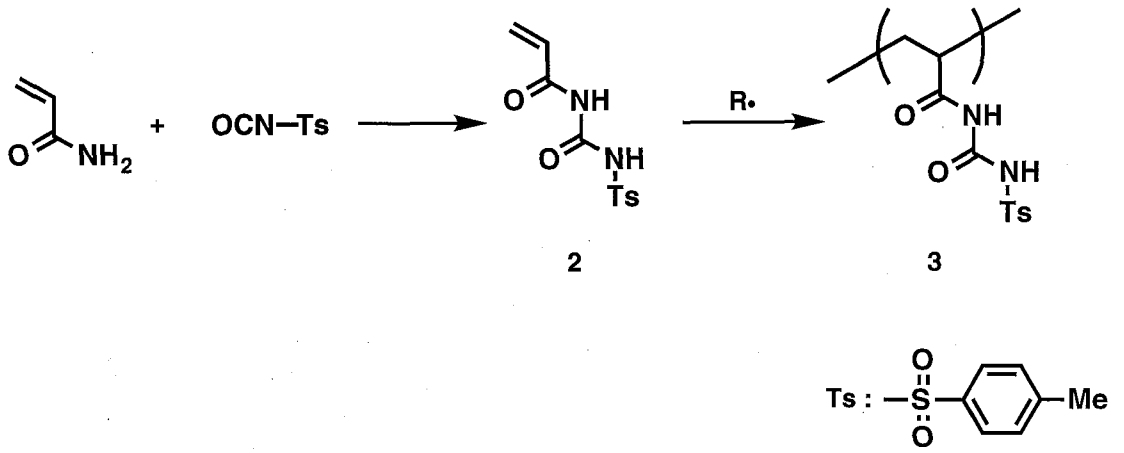
Scheme 1

In this chapter, more reactive *p*-toluenesulfonyl isocyanate [3] was employed as an "activated" isocyanate for the structural modification of acrylamide (Scheme 2). The radical polymerization of the resulting *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**2**) may produce polymer **3** having an arylsulfonyl urea moiety, which might show interesting reactivities. Accordingly, hydrolysis of the resulting polymer **3** is also described.



Scheme 2

2.2 Results and Discussion

Synthesis and Characterization of Monomer 2 and Polymer 3. Monomer **2** was synthesized by one-step reaction from *p*-toluenesulfonyl isocyanate and acrylamide in a good yield (87%). The IR spectrum of **2** showed two absorption bands at 1690 and 1726 cm^{-1} based on two carbonyl groups. In the ^1H NMR spectrum, the signals assignable to two NH protons were observed at low magnetic fields (δ 9.50 and 11.31 ppm) due to the electron-withdrawing character of the acylurea and the sulfonylurea groups.

The results of the radical polymerization is summarized in Table 1. Polymer **3** was obtained as a diethyl ether-insoluble part in good yields (83-94 %).[4] Polymer **3** is insoluble in ordinary organic solvents such as methylene chloride and tetrahydrofuran (THF), presumably due to the intermolecular hydrogen bondings, but soluble in polar solvents such as *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), and 1-methyl-2-pyrrolidone (NMP).

Table 1. Radical polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**2**).[a)]

Run	Solvent	Conc. (M)	Conv. (%)[b)]	Yield(%)[c)]	$\overline{M}_n(\overline{M}_w/\overline{M}_n)$[d)]
1	DMF	1.0	100	88	88000 (2.90)
2	DMSO	1.0	100	83	715000 (4.62)
3	NMP	1.0	100	94	30000 (1.59)

a) Monomer : 1 mmol, initiator : 2,2'-azobisisonitronitrile (AIBN, 3 mol%), 60°C, 10 h.
b) Determined by ^{1}H NMR spectrum.
c) Diethyl ether-insoluble part.
d) Estimated by GPC based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

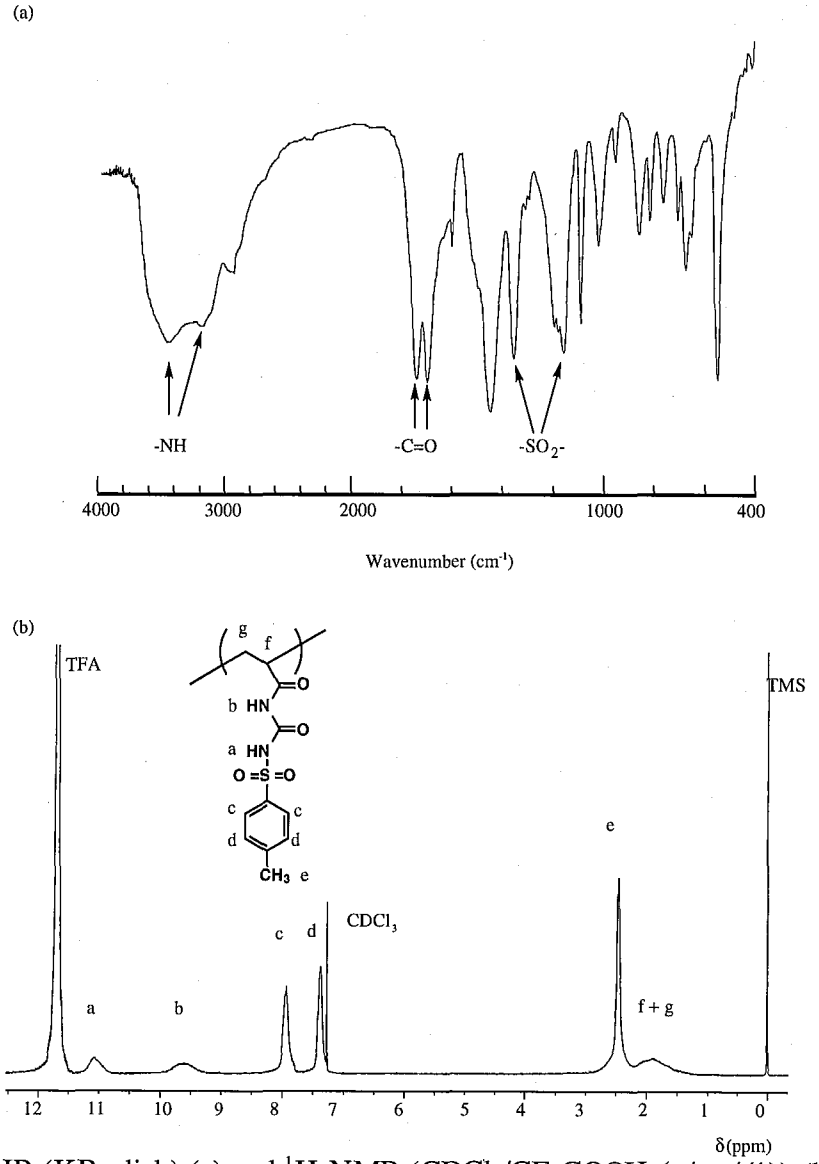


Figure 1 IR (KBr disk) (a) and ^{1}H-NMR ($CDCl_3/CF_3COOH$ (v/v=4/1)) (b) spectra of **3**.

The IR and ^{1}H NMR spectra of **3** (run 1) are shown Figure 1. The IR spectrum of **3** showed two absorption bands at 1701 and 1736 cm^{-1} based on two carbonyl groups. In the ^{1}H NMR spectrum, the signals ascribable to two NH protons were observed at low magnetic fields (δ 9.62 and 11.05 ppm) similar to the case of monomer **2**.[5)]

Thermal properties of polymer **3** was evaluated by thermogravimetric analysis (TGA) and differential scanning calorimetric (DSC) analysis. The 10% weight loss temperature (T_{d10}) of **3** was obtained at ca. 190°C from TGA,[6)] while the glass transition temperature (T_g) of **3** could not be observed in DSC below the decomposition temperature probably because of the restricted rotation of the polymer chain by the hydrogen bondings between the urea groups.

Copolymerization of 2 and MMA. Figure 2 shows the relationship between copolymer compositions and monomer feed ratios in the copolymerization of **2** (M_1) with methyl methacrylate (MMA) (M_2). By using the nonlinear least-squares analysis method (NLLS), monomer reactivity ratios were evaluated to be $r_1 = 2.41$ and $r_2 = 0.30$ from which the Alfrey-Price Q-e values of **2** were estimated as Q = 3.10 and e = 0.97. Although the reason for the rather large Q value (3.10) is not clear, the e value (0.97) reflects the electron-withdrawing character of the substituent in **2**.

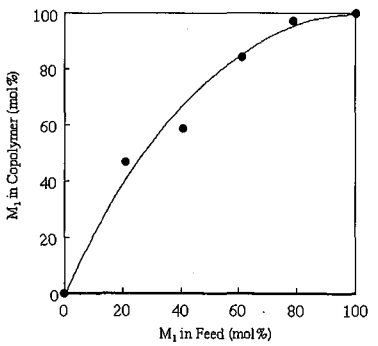


Figure 2 Copolymer composition curve of copolymerization of **2** (M_1) with MMA (M_2).

Hydrolysis of Poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) (3). Polymer **3** gradually became soluble in 1 *M* NaOH aqueous solution, and the obtained transparent solution was neutralized to give a white precipitate. ^{1}H NMR spectroscopy revealed that the recovered polymer undertook the partial hydrolysis (ca. 40% hydrolyzed). In the recovered precipitate, *p*-toluenesulfonylurea was also detected by the comparison of TLC with an authentic sample prepared from *p*-toluenesulfonyl isocyanate and ammonia. The production of *p*-toluenesulfonylurea may indicate that the polymer side chain can be hydrolyzed at the position of the carbonyl group connected to the polymer main chain. This is striking because hydrolysis of ordinary amides requires much higher temperature.

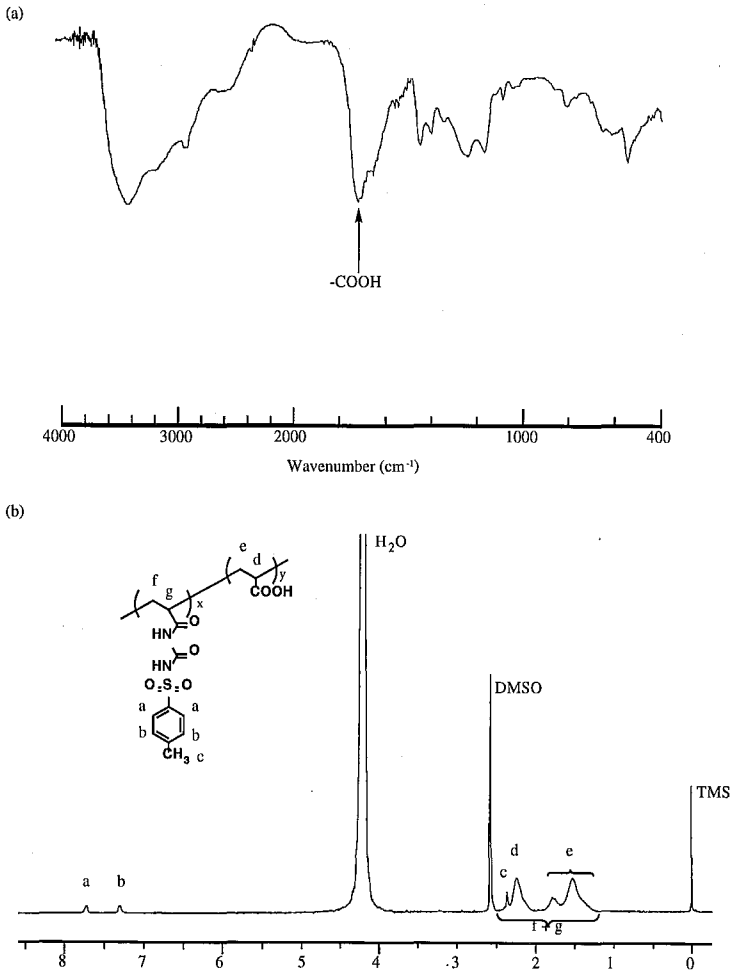
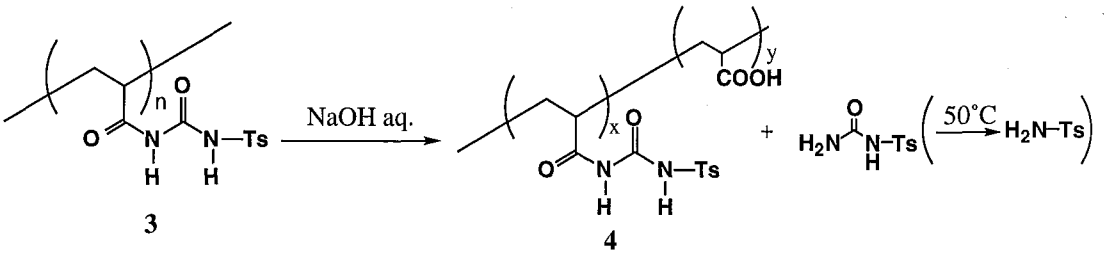


Figure 3 IR (KBr disk) (a) and ^{1}H-NMR (DMSO-d_6) (b) spectra of the polymer after hydrolysis at 50°C for 24 h.

Consequently, the polymeric product thus obtained was identified as polymer **4**, i.e., a copolymer of **2** with acrylic acid, whose unit ratio (x : y in Scheme 3) was evaluated as 4 : 6 on the basis of the ^{1}H NMR spectrum. In order to complete hydrolysis of **3**, the reaction was carried out at 50°C for 24h. The polymeric product was successfully isolated by dialysis. The IR and ^{1}H NMR spectra of the polymer obtained indicate that **3** was converted almost completely to poly(acrylic acid) (y unit-content: 97%, yield ~100%) (Figure 3). To isolate low-molecular weight products, the reaction mixture prepared independently under the same conditions was extracted with hot $CHCl_3$. ^{1}H NMR spectroscopy and TLC analysis revealed that the material extracted was a mixture of *p*-toluenesulfonylurea (65%) and *p*-toluenesulfonamide (35%) (yield ~100%). The latter is formed most probably by further hydrolysis of the former, because 89% of *p*-toluenesulfonylurea was hydrolyzed to *p*-toluenesulfonamide under the same reaction conditions.



Scheme 3

This hydrolysis process might not be restricted to the case of polymer **3** but generally applicable to hydrolysis of compounds having an *N*-acyl-*N'*-sulfonylurea group. From a point of view of a polymer drug, the

hydrolysis favorably results in releasing bioactive reagents such as sulfonylurea derivatives from the polymer chain. Additionally, from another point of view of synthetic utility, *p*-toluenesulfonyl isocyanate might act as a useful reagent to promote base catalyzed hydrolysis of amide group under mild conditions *via* urea intermediates.

2.3 Experimental

Materials. Methyl methacrylate (MMA), *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), and 1-methyl-2-pyrrolidone (NMP) were dried over CaH_2, distilled under reduced pressure, and stored under nitrogen atmosphere. Tetrahydrofuran (THF) was dried over sodium metal and distilled under nitrogen atmosphere. Other commercially available reagents were used without further purification.

Measurements. IR spectra were measured using a JASCO FT/IR-5300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a JEOL JNM-EX90 (^{1}H NMR: 90 MHz, ^{13}C NMR: 22.4 MHz) or a JEOL JNM-EX400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) spectrometer. Gel permeation chromatographic analyses were carried out on a Tosoh Co. HLC-8020 system (TSK® gel G6000HXL, TSK® gel G5000HXL, TSK® gel G4000HXL and TSK® gel G2500HXL (excluded volume of these columns corresponds to $\overline{M}_n = 4\times10^7$ of polystyrene), DMF containing LiBr (5.8 mM) as eluent, and an ultraviolet (UV) detector) using polystyrene as a standard. Thermal analyses were performed on Seiko Instruments TG/DTA220 and DSC220C. A glass transition temperature (T_g) by differential scanning calorimetry (DSC) was taken as an inflection point on a trace at a heating rate of 10 °C/min. A 10 % weight loss temperature (T_{d10}) was determined by thermogravimetric analysis (TGA) at a heating rate of 10 °C/min under

a nitrogen atmosphere.

Synthesis of *N*-Acryloyl-*N'*-*p*-toluenesulfonylurea (2). To a THF (180 mL) solution of acrylamide (10.31 g, 0.15 mol) and *N*-phenyl-*β*–naphtylamine (0.34 g, 1.55 mmol) as a radical inhibitor in a 500 mL round-bottomed flask equipped with a reflux condenser was added *p*-toluenesulfonyl isocyanate (28.60 g, 0.15 mol). The mixture was refluxed for 2 h under nitrogen atmosphere, and then evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from methanol. Yield 87%, mp. 162-163°C.

IR (KBr): 3412 (NH), 3245 (NH), 1726 (C=O), 1690 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.43 (s, 3H, $C\underline{H}_3$-C_6H_4-), 6.00 (d, J = 10.80 Hz , 1H, $C\underline{H}_2$=CH- *cis*), 6.13 (dd, J = 16.80 and 10.80 Hz, 1H, CH_2=$C\underline{H}$-), 6.57 (d, J = 16.80 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 7.31 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 7.93 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 9.50 (s, 1H, CON$\underline{H}$CO), 11.31 (s, 1H, CON$\underline{H}SO_2$) ppm; ^{13}C NMR (DMSO-d_6, 22.4 MHz), δ: 21.0, 127.8, 129.2, 129.6, 132.1, 135.6, 144.7, 148.6, 166.7 ppm; ANAL. Calcd for $C_{11}H_{12}N_2O_4S$: C, 49.25%; H, 4.51%; N, 10.44%; S, 11.95%. Found: C, 49.20%; H, 4.50%; N, 10.44%; S, 11.82%.

Radical Homopolymerization of 2. Monomer **2** (270 mg, 1 mmol) and 2,2'-azobisisobutylronitrile (AIBN, 5.0 mg, 0.03 mmol) were dissolved in DMF, DMSO, or NMP (1.0 mL) in a test tube, which was then degassed and sealed *in vacuo*. After 10 h at 60°C, the reaction mixture was poured into diethyl ether (ca. 50 mL) and the precipitated polymer was dried *in vacuo*.

IR (KBr): 3455 (NH), 3190 (NH), 1736 (C=O), 1701 (C=O) cm^{-1}; ^1H NMR($CDCl_3$/CF_3COOH = 4/1(v/v), 400 MHz) δ: 1.5-3.0 (m, 6H, -$C\underline{H}_2$-$C\underline{H}$- and $C\underline{H}_3$- C_6H_4-), 7.34 (s , 2H, -$C_6\underline{H}_4$-), 7.90 (s, 2H, -$C_6\underline{H}_4$-), 9.62 (bs, 1H, -CON$\underline{H}$CO-), 11.05 (bs ,1H, -CON$\underline{H}SO_2$-) ppm; ^{13}C NMR (DMSO-d_6, 100

MHz), δ: 21.1, 34.4, 41.2, 128.1, 129.7, 135.7, 144.8, 148.5, 177.4 ppm.

Copolymerization of 2 with MMA. The copolymerization of **2** with MMA were performed under various feed ratio. Typically, **2**, MMA, and AIBN (3 mol%) were dissolved in DMSO in a test tube, which was then degassed and sealed *in vacuo*. After 90 sec at 60°C, the reaction mixture was poured into diethyl ether and the precipitated polymer was dried *in vacuo* (yield; < 5%). The copolymer compositions were determined by their ^{1}H NMR spectra.

Hydrolysis of Poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) (3) at Room Temperature. The suspension of polymer **3** (1.02 g) in 1 *M* NaOH aq. (100 mL) was stirred at room temperature for 16 h. During this time, **3** was gradually dissolved and finally the mixture became a transparent solution. The resulting solution was slightly acidified with 2*M* HCl aq. (50 mL) to form a white precipitate, which was collected by centrifugation. The precipitate was washed three times with distilled water and subsequently dried *in vacuo* (0.94 g). TLC analysis and ^{1}H NMR spectrum indicated that this precipitate was a mixture of 40% hydrolyzed polymer **4** and *p*-toluenesulfonylurea (R_f = 0.54, chloroform : methanol = 4 : 1).

Hydrolysis of 3 at 50°C. Polymer **3** (0.25 g) in 1 *M* NaOH aq. (25 mL) was stirred at 50°C for 24 h. The reaction mixture was acidified with 2*M* HCl aq. (25 mL), concentrated to ca. 50 mL, and then subjected to dialysis using a cellulose tube (pore size 20 μm). The tube was kept in contact with stirred water for 24 h, and then the content was evaporated to give a polymeric product (yield 72.3 mg, ~100%).

IR (KBr): 3449 (OH), 1720 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6, 400MHz) δ: 1.28-1.95 (m, 2.0H, -C$\underline{H}_2$-CH-), 2.05-2.45 (m, 1.13H, -CH$_2$-C$\underline{H}$- and C$\underline{H}_3$-C$_6$H$_4$-) , 7.30 (bs, 0.11H, -C$_6\underline{H}_4$-), 7.74 (bs, 0.11H, -C$_6\underline{H}_4$-) ppm.

Independently, the reaction mixture prepared under the same conditions using **3** (0.25 g) was slightly acidified with 2 *M* HCl aq. (13 mL) and evaporated to dryness. The residual solid was successively refluxed with chloroform (50 mL, 7 times) to extract chloroform-soluble part. The combined chloroform solution was evaporated to dryness. TLC analysis and ^{1}H NMR spectrum indicated that the solid extracted (0.18 g) was a mixture of *p*-toluenesulfonylurea (35%; calculated by ^{1}H NMR spectrum) (R_f = 0.54, chloroform : methanol = 4 : 1) and *p*-toluenesulfonamide (65%; calculated by ^{1}H NMR spectrum) (R_f = 0.37, chloroform : methanol = 4 : 1) (yield ~100%).

References and Notes

1) H. Diefenbach and H. Ringsdorf, *Makromol. Chem.*, **131**, 247 (1970).
2) M. Kanamaru, T. Takata, and T. Endo, *J. Polym. Sci. : Part A: Polym. Chem.*, **33**, 1361 (1995)
3) H. Ulrich, *Chem. Rev.*, **65**, 369 (1965)
4) The molecular weight of polymer **3** was found to be dependent on the reaction solvents, which might be related to the difference in the chain-transfer constants of the solvents. See K. C. Berger and G. Brandrup, "Polymer Handbook", 3rd ed, J. Brandrup and E. H. Immergut Ed., pp II-98 and II-133.
5) Polymer **3** is insoluble in $CDCl_3$. Thus, trifluoroacetic acid (TFA) was added to dissolve the polymer.
6) The rather low decomposition temperature of **3** might be due to the reverse reaction path to the monomer synthesis to give the sulfonyl isocyanate and amide moieties.

Chapter 3

Reaction of *p*-Toluenesulfonyl Isocyanate with Polymers Having Amide Moieties and Hydrolysis of the Obtained Polymer

Abstract

The structural modification of polymers having amide moieties was carried out with *p*-toluenesulfonyl isocyanate. The resulting polymers revealed high hydrolytic character. For example, poly(acrylamide) was refluxed with an excess amount of *p*-toluenesulfonyl isocyanate in THF for 50 h to obtain a structurally modified polymer in 76% yield whose sulfonylurea functionality was 100%. The resulting polymer was subjected to hydrolysis in 1 *M* NaOH solution at 50°C to convert 90% of the sulfonylurea in the side chain to the carboxylic acid moieties.

3.1 Introduction

Modifications of monomers carrying active hydrogens with activated isocyanates may provide new monomers and consequently new polymers having unique functions. [1] In Chapter 2, the author has described the chemical modification of a vinyl monomer using sulfonyl isocyantes. [2] By the radical polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea which was prepared by the reaction of acrylamide with *p*-toluenesulfonyl isocyanate, a polymer having sulfonylurea moieties could be obtained in excellent yields. When the resulting polymer was hydrolyzed in 1 *M* NaOH aqueous solution, poly(acrylic acid) was smoothly obtained in a good yield by releasing a sulfonylurea derivative. Because *N*-acyl-*N'*-sulfonylurea derivatives can be easily obtained by the reaction of amides with sulfonyl isocyanate without any catalysts and are expected to be hydrolyzed to the corresponding carboxylic acids and sulfonylurea under mild basic conditions, the structural modification of polymers having amide moieties might proceed efficiently and the resulting polymers might reveal high hydrolytic character. In this chapter, the author wishes to describe the model studies and the hydrolytic properties of acylsulfonylurea derivatives from low molecular-weight amides with *p*-toluenesulfonyl isocyanate about the synthesis. Further, modification of polymers having amide moieties and hydrolysis of the obtained polymers is described as compared with the results from model experiments.

3.2 Results and Discussion

Model Reaction with Low Molecular-Weight Compounds. As reported by King,[3] the addition of *p*-toluenesulfonyl isocyanate with propionamide and with octanamide took place smoothly to give crystalline products of *N*-acyl-*N*'-*p*-toluenesulfonylureas (**1a** and **1b**, respectively) in high yields (91 and 95%, respectively) (Table 1, runs 1 and 2). Although the reactions of *p*-toluenesulfonyl isocyanate with *N*-alkylamides are reported not to be so clean as those with unsubstisuted amides,[3] *N*-butylpropionamide was found to react with *p*-toluenesulfonyl isocyanate to form **1c** in a quantitative yield when the reaction was carried out at ambient temperature (run 3).

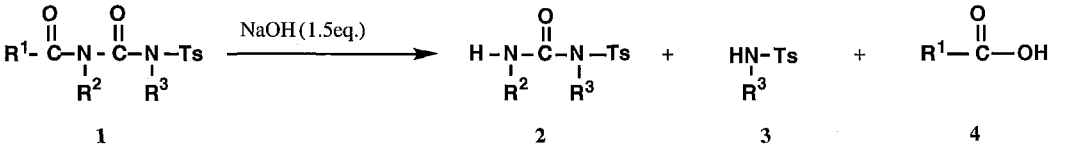
Table 1. Reaction of Low Molecular-Weight Amides with *p*-Toluenesulfonyl Isocyanate.

1

Run	R^1	R^2	Solvent	Temp.	Time (h)	Product	Yield (%)
1	**Et**	**H**	THF	Reflux	2	**1a**	91
2	**$CH_3(CH_2)_6$**	**H**	THF	Reflux	6	**1b**	95
3	**Et**	***n*-Bu**	Benzene	RT	36	**1c**	100

The obtained *N*-acyl-*N*'-*p*-toluenesulfonylureas (**1a-1c**) were subjected to hydrolysis in various conditions.

Table 2. Hydrolysis of **1** with NaOH.



1 **2** **3** **4**

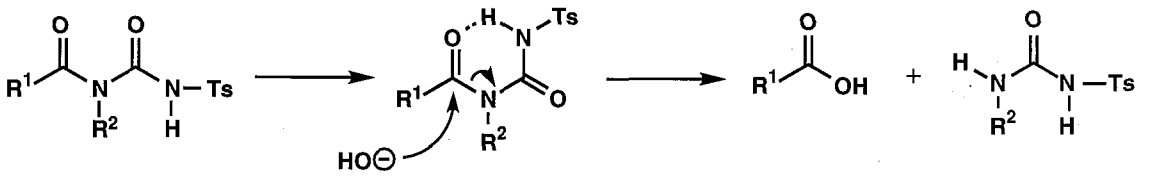
Run	substrate	R^1	R^2	R^3	Solvent	Temp.	Time (h)	Hydrolytic Product (Yield %) 2	3	4
1	**1a**	Et	H	H	H_2O	RT	16	83	0	—— a)
2	**1b**	$CH_3(CH_2)_6$	H	H	MeOH	Reflux	36	9	76	80
3	**1c**	Et	*n*-Bu	H	MeOH	RT	168	83	0	—— a)
4	**1c**	Et	*n*-Bu	H	MeOH	Reflux	9	84	0	—— a)

a) not determined.

When *N*-propionyl-*N'*-*p*-toluenesulfonylurea (**1a**) was hydrolyzed in 1 *M* NaOH aqueous solution at room temperature for 16 h, *p*-toluenesulfonylurea was isolated in 83% yield which was identified by comparing its R_f value and ^1H NMR spectrum with those of an authentic sample (Table 2, run 1). In this case, however, propionic acid which should be generated as another component was not detected, probably because of its low boiling point to be evaporated during the work up process. *N*-*n*-Octanoyl-*N'*-*p*-toluenesulfonylurea (**1b**) was hydrolyzed in refluxing methanol with NaOH to give *p*-toluenesulfonylurea (9%), *p*-toluenesulfonamide (76%), and also octanoic acid (80%) (run 2). The lower yield of *p*-toluenesulfonylurea, and alternatively higher yield of *p*-toluenesulfonamide which was the identical R_f value and ^1H NMR spectrum with an authentic sample are due to the forced reaction conditions. As described in Chapter 2, 89% of *p*-toluenesulfonylurea was found to be hydrolyzed to *p*-toluenesulfonamide by using NaOH at 50°C for 24 h.[6] Therefore, *p*-toluenesulfonylurea initially formed by hydrolysis of **1b** might be hydrolyzed to *p*-toluenesulfonamide under the examined conditions. The hydrolysis of *N*-propionyl-*N*-*n*-butyl-*N'*-*p*-

toluenesulfonylurea (**1c**) was carried out at room temperature for 168 h. Consequently, *N*-*n*-butyl-*N'*-*p*-toluenesulfonylurea was isolated in 83% yield whose R_f value and ^1H NMR spectrum were also consistent with those of an authentic sample (run 3). *N*-*n*-Butyl-*N'*-*p*-toluenesulfonylurea was also produced in 84% yield by refluxing **1c** for 9 h in 1 *M* NaOH methanol solution (run 4).

N-Acyl-*N'*-*p*-toluenesulfonylurea derivatives (**1a**-**1c**) were found to be hydrolyzed by the chemoselective nucleophilic attack to the amide-carbonyl group. This selectivity might be originated from the intramolecular-hydrogen bonding between the N-H adjacent to the sulfonyl group and the oxygen of the amide-carbonyl group. Owing to the increase in δ^+ character of the amide-carbonyl group, *N*-acyl-*N'*-*p*-toluenesulfonylurea derivatives might be easily attack by hydroxide anion chemoselectively at this position (Scheme 1).



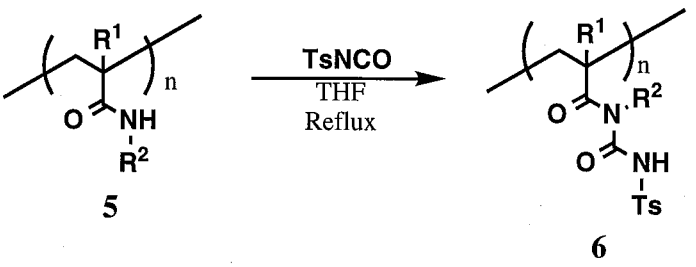
Scheme 1

From the above results on the model studies, it was found that *N*-acyl-*N'*-*p*-toluenesulfonylureas can be obtained easily from *p*-toluenesulfonyl isocyanate and amide derivatives in excellent yields. Moreover, *N*-acyl-*N'*-*p*-toluenesulfonylureas were found to reveal high hydrolytic character under mild basic conditions to give the corresponding carboxylic acids and *p*-toluenesulfonylurea or *p*-toluenesulfonamide. Accordingly, it is expected that polymer reactions starting from poly(acrylamide) as well as its derivatives would proceed effectively and

that the resulting polymers must reveal high hydrolytic character.

Reaction of *p*-Toluenesulfonyl Isocyanate with Polymers Having Amide Moieties. Poly(acrylamide) derivatives (**5a-5c**) were prepared by the radical polymerization of acrylamide, methacrylamide, and *N*-butylacrylamide using AIBN (3 mol%) as an initiator and 1-dodecanethiol as a chain-transfer agent. Table 3 summarizes the results on the reaction of *p*-toluenesulfonyl isocyanate with polymers having amide moieties (**5a-5c**). When a THF solution of poly(acrylamide) (**5a**, $\overline{P_n}$ = 14.10) and excess of *p*-toluenesulfonyl isocyanate were refluxed for 50 h, poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) (**6a**) was obtained in 76% yield. The ^{1}H NMR spectrum of the produced polymer indicated that the polymer reaction with *p*-toluenesulfonyl isocyanate was quantitative (Figure 1). Similarly, polymers **5b** and **5c** reacted with *p*-toluenesulfonyl isocyanate quantitatively to introduce the sulfonylurea moieties in the side chain.

Table 3. Reaction of *p*-Toluenesulfonyl Isocyanate with Polymers Having Amide Moieties.



5 **6**

Run	Amide	R^1	R^2	$\overline{P_n}$	Time (h)	Adduct	Yield (%)
1	**5a**	**H**	**H**	14.10	50	**6a**	76
2	**5b**	**Me**	**H**	4.11	96	**6b**	61
3	**5c**	**H**	***n*-Bu**	2.96	96	**6c**	96

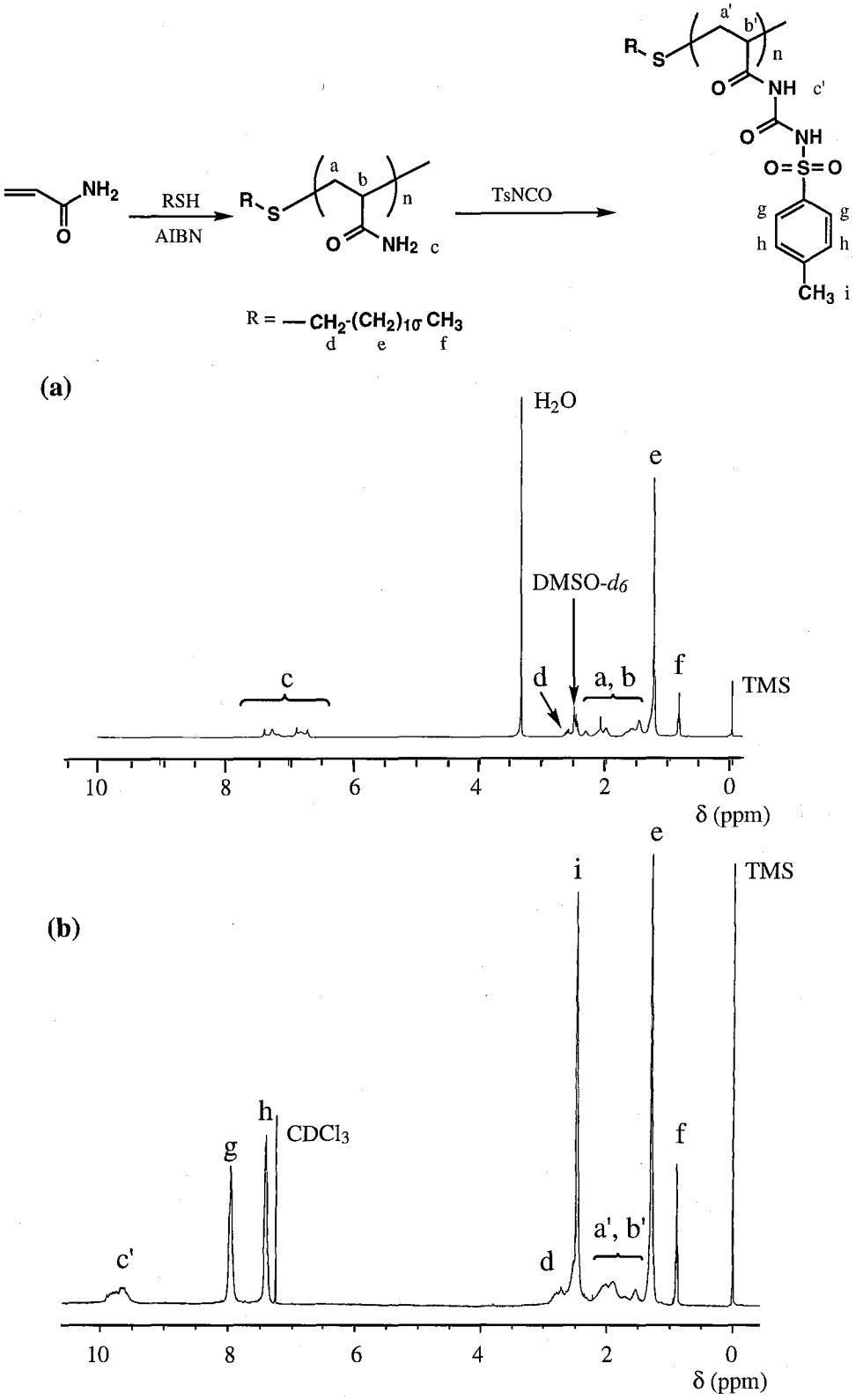
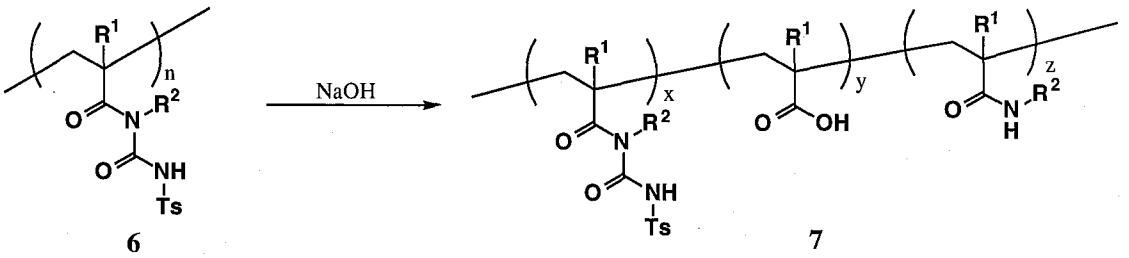


Figure 1 ^{1}H NMR spectra of **5a** in DMSO-d_6 (a) and **6a** in $CDCl_3/CF_3COOH$ (v/v=4/1) (b).

Hydrolysis of Polymer Having Sulfonylurea Moieties by Using 1 *M* NaOH Solution. Hydrolysis of polymers **6a-6c** was carried out with 1 *M* NaOH solution in several conditions (Table 4).

Table 4. Hydrolysis of Polymers Having Sulfonylurea Moieties by using 1*M* NaOH Solution.



6 7

Run	Substrate	R^1	R^2	Solvent	Temp. (°C)	Time (h)	Hydrolytic Product	Yield (%)	x / y / z
1	**6a**	**H**	**H**	H_2O	RT	48	**7a**	100	50 / 50 / 0
2	**6a**	**H**	**H**	H_2O	50	24	**7a**	84	10 / 90 / 0
3	**6a**	**H**	**H**	H_2O	50	52	**7a**	90	10 / 90 / 0
4	**6b**	**Me**	**H**	H_2O	50	52	**7b**	80	18 / 82 / 0
5	**6c**	**H**	***n*-Bu**	MeOH	50	72	**7c**	78	10 / 0 / 90

By the hydrolysis of polymer **6a** at room temperature for 48 h in 1 *M* NaOH aqueous solution, polymer **7a** was obtained in 100% yield whose unit ratio was determined as x / y / z = 50 / 50 / 0 by the ^{1}H NMR spectrum (run 1). When **6a** was hydrolyzed at 50°C for 24 h, the remaining sulfonylurea moieties in **7a** decreased to 10% (run 2). To obtain the polymer solely having the carboxylic acid unit (i.e., y unit), the hydrolysis was carried out for prolonged period (i.e., 52 h) (run 3). However, the degree of hydrolysis did not become higher than 90%. In the ^{1}H NMR spectrum of **6a** (Figure 2a), the aromatic and the methyl protons in the tosyl group are observed at δ 7.20-8.20 (g, h) and 2.45 (i) ppm, respectively. The corresponding signals become very small in the ^{1}H NMR spectrum of the polymer after hydrolysis **7a** (run 2, Figure 2b). The formation of the carboxylic acid moieties could

be further supported by the absorption band at 1719 cm^{-1} in the IR spectrum of **7a** (Figure 3).

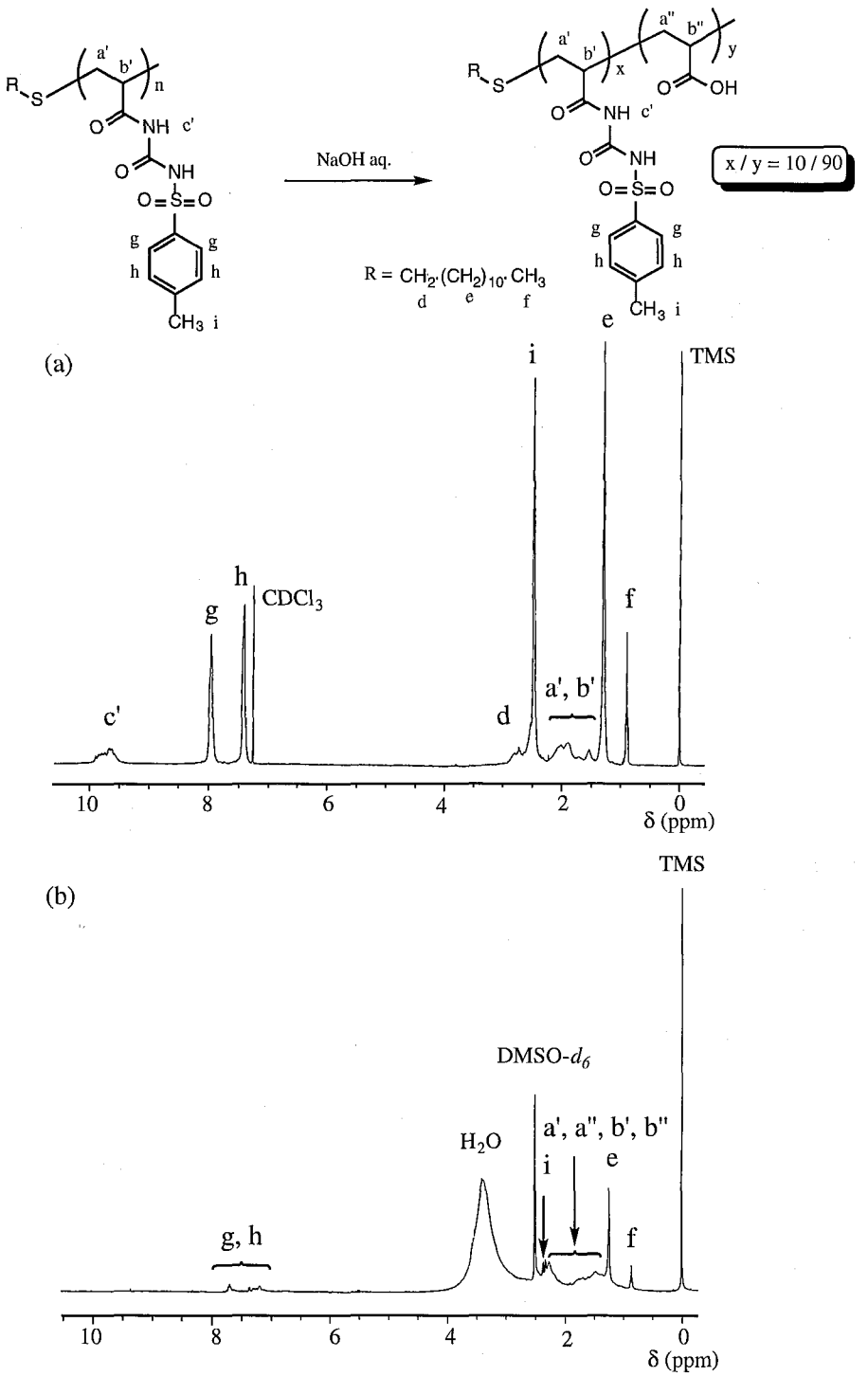


Figure 2 ^{1}H NMR spectra of **6a** in $CDCl_3/CF_3COOH$ (v/v=4/1) (a) and **7a** in DMSO-d_6 (b).

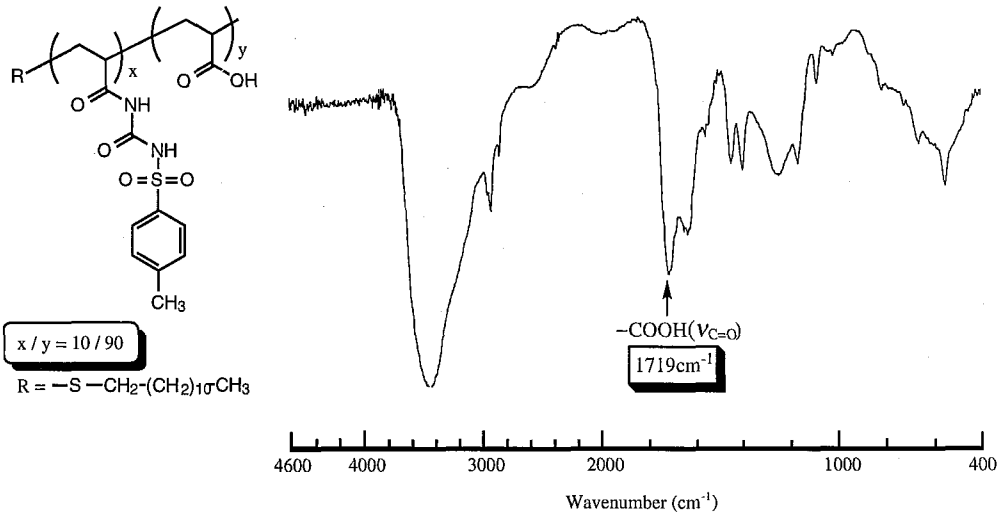


Figure 3 IR spectra of **7a** (KBr disk).

Likewise, polymer **6b** was subjected to hydrolysis at 50°C for 52 h in 1 *M* NaOH aqueous solution to afford **7b** which contained 18% of the starting sulfonylurea moieties (run 4). In the case of polymer **6c**, the hydrolysis at 50°C for 72 h in 1 *M* NaOH methanol solution afforded polymer **7c** and *p*-toluenesulfonamide, which were isolated by recycling preparative HPLC. In the ^{1}H NMR spectrum, polymer **7c** was found to have the unreacted x unit (10%) and z unit (90%).

Although the results of the hydrolysis of **6a** and **6b** coincided with those of the model reactions where the *N*-acyl-*N'*-*p*-toluenesulfonylurea moiety was chemoselectively hydrolyzed to the carboxylic acid moieties, **6c** was found to undertake hydrolysis at the different position, i.e., at the carbonyl group adjacent to the TsNH group. Although the reason for the specific hydrolysis in the case of **6c** is not clear, steric hindrance and/or the hydrophobicity of the butyl group and the main chain of the polymer might make it difficult to cause the nucleophilic attack at the amide-carbonyl group. Consequently, the nucleophilic attack of hydroxide might take place selectively toward the carbonyl group adjacent to TsNH group.

3.3 Experimental

Materials. Acrylamide and methacrylamide were recrystallized from benzene. Methanol was distilled from magnesium methoxide under nitrogen atmosphere. Acetonitrile was dried over CaH_2, distilled, and stored under nitrogen. Other commercially available reagents were used without further purification.

Measurements. IR spectra were measured on a JASCO FT/IR-5300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-EX90 (^{1}H NMR: 90 MHz and ^{13}C NMR: 22.4 MHz) or JEOL JNM-EX400 (^{1}H NMR: 400 MHz and ^{13}C NMR: 100 MHz) spectrometer. Products obtained by hydrolysis were purified by Japan Analytical Industry Co., Ltd. recycling preparative HPLC system equipped with polystyrene gel columns (JAIGEL-1H and JAIGEL-2H) using chloroform as eluent. Fast atom bombardment mass spectra (FAB/MS) were recorded by using a JEOL JMS-700 spectrometer, whereby a mixture of a sample and *m*-nitrobenzyl alcohol on a standard FAB target was subjected to a beam of xenon atoms produced at 6 keV, 2 mA.

Synthesis of *N*-Propionyl-*N'*-*p*-toluenesulfonylurea (1a). To a 500 mL round bottomed flask containing a THF (150 mL) solution of propionamide (9.27 g, 0.13 mol) was added *p*-toluenesulfonyl isocyanate (25.80 g, 0.13 mol) under nitrogen. After refluxing for 2 h, the reaction mixture was evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from methanol. Yield 91% (30.99 g, 0.12 mol), mp. 123°C, R_f = 0.73 (chloroform / methanol = 4/1 v/v).

IR (KBr): 3420 (NH), 3250 (NH), 2982, 2942 (CH_3, -CH_2-), 1746 (C=O), 1696 (C=O), 1370 (-SO_2-), 1161 (-SO_2-), 554 (N-C=O)cm^{-1}; ^{1}H NMR (DMSO-d_6, 90 MHz) δ: 1.00 (t, J = 7.74 Hz, 3H, C$\underline{H}_3$CH$_2$-), 2.11-2.46 (m,

2H, $CH_3C\underline{H}_2$-), 2.41 (s, 3H, $C\underline{H}_3$-C_6H_4-), 7.44 (d, J = 8.64 Hz, 2H, -$C_6\underline{H}_4$-), 7.89 (d, J= 8.64 Hz, 2H, -$C_6\underline{H}_4$-), 10.84 (bs, 1H, -CON<u>H</u>CO-), 11.33 (bs, 1H, -CON<u>H</u>SO_2-) ppm; ^{13}C NMR (DMSO-d_6, 22.4 MHz) δ: 8.15 20.99, 29.06, 127.76, 129.52, 135.74, 144.55, 148.33, 176.90 ppm; FAB/MS *m/z* 271 $[M+H]^+$.

Synthesis of *N*-*n*-Octanoyl-*N'*-*p*-toluenesulfonylurea (1b). To a 100 mL round bottomed flask containing a THF (50 mL) solution of *n*-octanamide (2.10 g, 14.70 mmol) was added *p*-toluenesulfonyl isocyanate (2.92 g, 14.80 mmol) under nitrogen. After refluxing for 6 h, the reaction mixture was evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from a mixture of hexane-chloroform. Yield 95% (4.74 g, 13.90 mmol), mp. 112°C, R_f = 0.50 (chloroform / methanol = 9/1 v/v).

IR (KBr): 3439 (NH), 3248 (NH), 2959, 2926, 2857 (CH_3, -CH_2-), 1746 (C=O), 1688 (C=O), 1370 (-SO_2-), 1159 (-SO_2-), 554 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.89 (t, J = 6.80 Hz, 3H, $C\underline{H}_3CH_2$-), 1.20-1.40 (m, 8H, -$C\underline{H}_2$-), 1.58-1.70 (m, 2H, -$C\underline{H}_2$-CH_2-CO-), 2.30 (t, J= 7.20 Hz, 2H, -$C\underline{H}_2$-CO-), 2.43 (s, 3H, $C\underline{H}_3$-C_6H_4-), 7.31 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 7.92 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 9.14 (bs, 1H, -CON<u>H</u>CO-), 11.20 (bs, 1H, -CON<u>H</u>SO_2-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 14.06, 21.71, 22.59, 24.45, 28.93, 28.97, 31.62, 36.92, 128.60, 129.48, 135.61, 145.23, 149.89, 175.51 ppm; FAB/MS *m/z* 341 $[M+H]^+$.

Synthesis of *N*-Propionyl-*N*-*n*-butyl-*N'*-*p*-toluenesulfonyl urea (1c). To a 500 mL round bottomed flask containing a benzene (200 mL) solution of propionyl chloride (25.00 g, 0.27 mol) was added *n*-butylamine (130 mL, 2.40 mol) at 0°C under nitrogen. After stirring at room temperature for 1 h, the reaction mixture was washed with water, 10% citric acid aqueous solution, and saturated $NaHCO_3$ aqueous solution.

The organic layer was dried and evaporated to afford essentially pure *N*-*n*-butyl-propionamide (8.11 g, 24%) as a colorless oil which was used in the next step without further purification.

IR (neat): 3299 (NH), 2963, 2934, 2876 (CH_3, -CH_2-), 1647 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 0.92 (t, J = 7.20 Hz, 3H, $C\underline{H}_3CH_2$-), 1.15 (t, J = 7.60 Hz, 3H, $C\underline{H}_3CH_2$-), 1.35 (dt, J = 14.40 and 7.20 Hz, 2H, $CH_3C\underline{H}_2CH_2CH_2$-), 1.48(dt, J = 14.40 and 7.20 Hz, 2H, $CH_3CH_2C\underline{H}_2CH_2$-), 2.21 (dd, J = 15.20 and 7.20 Hz, 2H,-N-$C\underline{H}_2$-), 3.24 (dd, J = 14.40 and 7.20 Hz, 2H,-CO-$C\underline{H}_2$-), 6.02 (bs, 1H, -N$\underline{H}$-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 10.02, 13.79, 20.12, 29.74, 31.77, 39.25, 173.96 ppm; FAB/MS *m/z* 130 $[M+H]^+$.

To a 50 mL round bottomed flask containing a benzene (20 mL) solution of *N*-*n*-butyl-propionamide (1.82 g, 14.10 mmol) was added *p*-toluenesulfonyl isocyanate (2.79 g, 14.20 mmol) under nitrogen. After stirring at room temperature for 36 h, the reaction mixture was concentrated and the residue was purified by chromatography on silica gel with chloroform as eluent to isolate **3** as a pale yellow oil. Yield 100% (4.60 g, 14.10 mmol), R_f = 0.68 (chloroform / methanol = 9/1 v/v).

IR (neat): 3412 (NH), 2963, 2934, 2875 (CH_3, -CH_2-), 1723 (C=O), 1672 (C=O), 1354 (-SO_2-), 1169 (-SO_2-), 548 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 0.85-0.95 (m, 3H, $C\underline{H}_3CH_2$-), 1.10-1.20 (m, 3H, $C\underline{H}_3CH_2$-), 1.20-1.40 (m, 2H, $CH_3C\underline{H}_2CH_2CH_2$-), 1.40-1.60 (m, 2H, $CH_3CH_2C\underline{H}_2CH_2$-), 2.40-2.47 (m, 3H, $C\underline{H}_3CH_4$-), 2.52-2.63 (m, 2H, -N-$C\underline{H}_2$-), 3.55-3.65 (m, 2H,-CO-$C\underline{H}_2$-), 7.29-7.37 (m, 2H, -$C\underline{H}_4$-), 7.90-8.00 (m, 2H, -$C\underline{H}_4$-), 12.21 (bs, 1H, -CON$\underline{H}SO_2$-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 8.64, 13.50, 19.91, 20.99, 29.40, 31.08, 44.21, 128.41, 129.40, 135.92, 144.70, 149.90, 178.66 ppm; FAB/MS *m/z* 327 $[M+H]^+$.

Hydrolysis of *p*-Toluenesulfonylurea Derivatives (1a-1c). *p*-Toluenesulfonylurea derivatives (**1a-1c**) (1.0 *M*) were dissolved in 1 *M* NaOH aqueous (or methanol) solution (1.5 eq.). After the reaction, the mixture was slightly acidified by 1 *M* HCl aqueous solution. The resulting mixture was evaporated to dryness and chloroform was added to the residue. Insoluble inorganic salt was removed by filtration and the filtrate was evaporated to dryness. The residue was subjected to chromatography on silica gel with chloroform as eluent to isolate hydrolyzed products which were identified by ^{1}H NMR spectra, TLC analyses, and FAB/MS spectra by comparing those of authentic samples.

Synthesis of Authentic Samples.

Synthesis of *p*-Toluenesulfonylurea. To a 100 mL round bottomed flask containing a acetonitrile (50 mL) solution of *p*-toluenesulfonyl isocyanate (2.73 g, 13.80 mmol) was bubbled a large excess of NH_3 gas at 0°C. After stirring at room temperature for additional 1 h, the reaction mixture was evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from a mixture of water and ethanol. Yield 80% (2.36 g, 11.00 mmol), mp. 174-176°C, R_f = 0.38 (chloroform / methanol = 9/1 v/v).

IR (KBr): 3331 (NH), 3206 (NH), 1655 (C=O), 1375 (-SO_2-), 1169 (-SO_2-) cm^{-1}; ^{1}H NMR (DMSO-d_6, 90 MHz) δ: 2.39 (s, 3H, C$\underline{H}_3$CH_4-), 6.33 (bs, 2H, -CO-N$\underline{H}_2$), 7.40 (d, J= 8.01 Hz, 2H, -C$\underline{H}_4$-), 7.78 (d, J= 8.01 Hz, 2H, -C$\underline{H}_4$-), 10.48 (bs, 1H, -CON$\underline{H}$SO_2-) ppm; ^{13}C NMR (DMSO- d_6, 22.4 MHz) δ: 22.40, 127.09, 129.34, 137.41, 143.49, 151.99 ppm; FAB/MS *m/z* 215 $[M+H]^+$.

Synthesis of *p*-Toluenesulfonamide. To a 50 mL round bottomed flask containing 2 mL THF and 2 mL H_2O was added *p*-toluenesulfonyl isocyanate (0.51 g, 2.58 mmol) at 0°C. After stirring at

room temperature for 10 min, the reaction mixture was evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from a mixture of benzene and methanol. Yield 87% (0.38 g, 2.24 mmol), mp 138-139°C, R_f = 0.55 (chloroform / methanol = 9/1 v/v). IR (KBr): 3329 (NH), 3243 (NH), 1327 (-SO_2-), 1152 (-SO_2-) cm^{-1}; ^{1}H NMR (DMSO-d_6, 90 MHz) δ: 2.38 (s, 3H, C$\underline{H}_3$CH$_4$-), 7.24 (bs, 2H, - SO_2-N$\underline{H}_2$), 7.35 (d, J = 8.06 Hz, 2H, -C$\underline{H}_4$-), 7.72 (d, J = 8.06 Hz, 2H, -C$\underline{H}_4$-) ppm; ^{13}C NMR (DMSO-d_6, 22.4 MHz) δ: 20.82, 125.55, 129.17, 141.38, 141.71 ppm; FAB/MS *m/z* 172 $[M+H]^+$.

Synthesis of *N*-*n*-Butyl-*N'*-*p*-toluenesulfonylurea. To a 50 mL round bottomed flask containing a benzene (20 mL) solution of *p*-toluenesulfonyl isocyanate (1.33 g, 6.72 mmol) was added *n*-butylamine (1.0 mL, 18.50 mol) at 0°C under nitrogen. After stirring at room temperature for 1 h, the reaction mixture was washed with water, 10% citric acid aqueous solution, and saturated $NaHCO_3$ aqueous solution. The organic layer was dried over $MgSO_4$, and evaporated to dryness. The obtained white solid was recrystallized from a mixture of H_2O and methanol. Yield 62% (1.12 g, 4.15 mmol), mp 109°C, R_f = 0.70 (chloroform / methanol = 9/1 v/v).

IR (KBr): 3339 (NH), 3171 (NH), 1661 (C=O), 1346 (-SO_2-), 1165 (-SO_2-) cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ: 0.95 (t, J = 6.48 Hz, 3H, C$\underline{H}_3$CH$_2$-), 1.10-1.90 (m, 4H, CH$_3$ C$\underline{H}_2$ C$\underline{H}_2$CH$_2$-), 2.49 (s, 3H, C$\underline{H}_3$CH$_4$-), 3.28 (dd, J = 12.51 and 6.75 Hz, 2H, -C$\underline{H}_2$-NHCO-), 6.60 (bs, 1H, -CH$_2$-N$\underline{H}$CO-), 7.36 (d, J = 8. 37 Hz, 2H, -C$\underline{H}_4$-), 7.83 (d, J = 8.37 Hz, 2H, -C$\underline{H}_4$-), 8.75 (bs, 1H, -SO_2-N$\underline{H}$-CO-) ppm; ^{13}C NMR ($CDCl_3$, 22.4 MHz) δ: 13.60, 19.77, 21.55, 31.50, 39.97, 126.94, 129.79, 136.77, 144.56, 152.09 ppm; FAB/MS *m/z* 271 $[M+H]^+$.

Radical Polymerization of Acrylamide, Methacrylamide, and *N*-*n*-Butylacrylamide (Typical Procedure). Monomer (acrylamide, methacrylamide, or *N*-*n*-butylacrylamide) (1.0 *M*), 2,2'-azobisisobutylronitrile (AIBN, 3 mol%), and 1-dodecanethiol (34, 10 or 32 mol%, respectively) were dissolved in methanol in a round bottomed flask, which was then degassed *in vacuo*. After the reaction at 60°C for 5 h, 12 h, or 24 h, respectively, under nitrogen, the reaction mixture was poured into diethyl ether (in the case of acrylamide or methacrylamide) or water (in the case of *N*-*n*-Butylacrylamide) and the precipitated polymer was dried *in vacuo*.

Poly(acrylamide) (5a). Yield 45%, $\overline{P_n}$ = 14.10, IR (KBr): 3374 (NH), 3200 (NH), 2922, 2853 (CH_3-, -CH_2-), 1661 (C=O) cm^{-1}; ^1H NMR(DMSO-d_6, 400 MHz) δ: 0.86 (t, J = 6.80 Hz, 3H×0.071, C$\underline{H}_3$-CH_2-), 1.10-1.25 (m, 20H×0.071, -(C$\underline{H}_2$)$_{10}$-), 1.25-1.83 (m, 2H, -C$\underline{H}_2$-CH-), 1.83-2.49 (m, 1H, -CH_2-C$\underline{H}$-), 2.55-2.70 (m, 2H×0.071, -S-C$\underline{H}_2$-), 6.60-7.20 (m, 2H, N$\underline{H}_2$) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz), δ: 13.95, 22.11, 26.95, 28.25, 28.64, 28.71, 29.02, 29.09, 31.05, 31.05, 31.31, 35.62, 172.62, 173.92, 176.66 ppm.

Poly(methacrylamide) (5b). Yield 47%, $\overline{P_n}$ = 4.11, IR (KBr): 3418 (NH), 3214 (NH), 2924, 2855 (CH_3-, -CH_2-), 1663 (C=O) cm^{-1}; ^1H NMR(DMSO-d_6, 400 MHz) δ: 0.86 (t, J = 6.80 Hz, 3H×0.243, C$\underline{H}_3$-CH_2-), 0.89-1.16 (m, 3H, -CH_2-C(C$\underline{H}_3$)-), 1.16-1.33 (m, 20H×0.243, -(C$\underline{H}_2$)$_{10}$-), 1.33-2.10 (m, 2H, -C$\underline{H}_2$-C(CH_3)-), 2.55-2.70 (m, 2H×0.243, -S-C$\underline{H}_2$-), 6.45-7.50 (m, 2H, N$\underline{H}_2$) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 13.95, 17.88, 18.43, 20.85, 22.11, 28.25, 28.71, 28.88, 29.02, 29.41, 31.31, 33.14, 35.22, 35.62, 41.31, 44.60, 44.86, 45.21, 45.50, 45.70, 45.88, 46.07, 46.40, 177.59, 177.78, 177.94, 178.34, 178.96, 179.15, 179.33, 180.15 ppm.

Poly(*N*-*n*-butylacrylamide) (5c). Yield 99%, $\overline{P_n}$ = 2.96, IR (KBr): 3436 (NH), 3293 (NH), 2957, 2924, 2853 (CH_3-, -CH_2-), 1645 (C=O) cm^{-1}; ^{1}H NMR(DMSO-d_6, 400 MHz) δ: 0.82-0.92 (m, 3H×0.338, C$\underline{H}_3$-$(CH_2)_{11}$S-, 3H, C$\underline{H}_3$-$(CH_2)_3$-N-), 1.17-1.80 (m, 20H×0.338, -$(C\underline{H}_2)_{10}$-, 4H, CH_3-$(C\underline{H}_2)_2$-CH_2-N-, and 2H, -C$\underline{H}_2$-CH-), 1.80-2.48 (m, 1H, -CH_2-C$\underline{H}$-), 2.55-2.68 (m, 2H×0.338, -S-C$\underline{H}_2$-), 2.90-3.13 (m, 2H, CONH-C$\underline{H}_2$-), 7.20-8.20 (m, 1H, N$\underline{H}$) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 13.60, 13.88, 19.53, 19.64, 22.07, 24.41, 27.17, 28.22, 28.60, 28.69, 28.98, 31.00, 31.22, 31.27, 33.10, 33.70, 35.92, 38.11, 45.70, 170.19, 171.30, 171.48, 172.87, 173.00, 173.75, 173.94 ppm.

Reaction of *p*-Toluenesulfonyl Isocyanate with Polymers Having Amide Moieties (Typical Procedure). To a 50 mL round bottomed flask containing a THF solution of polyacrylamide derivatives (**5a**: 4.24 m*M*, **5b**: 18.40 m*M*, or **5c**: 17.60 m*M*, respectively) was added a large excess of *p*-toluenesulfonyl isocyanate under nitrogen. After 50 h (**5a**) or 96 h (**5b**, **5c**), the mixture was treated with methanol and evaporated to dryness. The residue was dissolved in methanol, and the resulting solution was poured into hexane-diethyl ether (1/1 v/v), methanol-water (1/4 v/v), or water, respectively. The precipitated polymer was filtered and dried *in vacuo*.

Poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) (6a). Yield 77%, IR (KBr): 3455 (NH), 3177 (NH), 2926, 2855 (CH_3, -CH_2-), 1736 (C=O), 1699 (C=O), 1358 (-SO_2-), 1159 (-SO_2-), 548 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$ / TFA = 4/1 v/v, 400 MHz) δ: 0.88 (t, *J*= 6.40 Hz, 3H×0.071, C$\underline{H}_3$-CH_2-), 1.10-1.26 (m, 20H×0.071, -$(C\underline{H}_2)_{10}$-), 1.26-1.93 (m, 2H, -C$\underline{H}_2$-CH-), 1.93-2.64 (m, 1H, -CH_2-C$\underline{H}$-), 2.45 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.64-2.90 (m, 2H×0.071, -S-C$\underline{H}_2$-), 7.20-7.60 (m, 2H, -$C_6\underline{H}_4$-), 7.70-8.20 (m, 2H, -$C_6\underline{H}_4$-), 9.20-10.10 (m, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ:

13.92, 21.07, 22.05, 28.14, 28.55, 28.67, 28.97, 31.27, 32.81, 41.31, 125.60, 127.85, 129.64, 135.57, 144.75, 148.24, 175.29, 176.33, 177.41, 177.65 ppm.

Poly(*N*-methacryloyl-*N'*-*p*-toluenesulfonylurea) (6b). Yield 58%, IR (KBr): 3449 (NH), 3246 (NH), 2926, 2855 (CH_3, -CH_2-), 1720 (C=O), 1698 (C=O), 1358 (-SO_2-), 1163 (-SO_2-), 550 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$ / TFA = 4/1 v/v, 400 MHz) δ: 0.80-1.00 (m, 3H×0.24, C$\underline{H}_3$-CH_2-), 1.10-2.80 (m, 3H, -CH_2-C(C$\underline{H}_3$)-, 20H×0.24, -(C$\underline{H}_2$)$_{10}$-, 2H, -C$\underline{H}_2$-C(CH_3)-, and 2H×0.24, -S-C$\underline{H}_2$-), 2.49 (s, 3H, C$\underline{H}_3$-C_6H_4-), 7.30-7.60 (m, 2H, -$C_6$$\underline{H}_4$-), 7.70-8.20 (m, 2H, -$C_6$$\underline{H}_4$-), 9.20-10.00 (m, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 13.88, 21.05, 22.05, 23.21, 28.03, 28.33, 28.51, 28.66, 28.70, 29.22, 31.25, 34.32, 36.30, 38.05, 41.23, 52.80, 124.87, 125.58, 127.39, 127.76, 127.89, 128.62, 129.15, 129.24, 129.62, 135.60, 136.28, 141.40, 141.79, 144.20, 144.71, 148.53, 151.55, 177.19, 179.28 ppm.

Poly(*N*-acryloyl-*N*-*n*-butyl-*N'*-*p*-toluenesulfonylurea) (6c). Yield 82%, IR (neat): 3322 (NH), 2957, 2927, 2855 (CH_3, -CH_2-), 1752 (C=O), 1651 (C=O), 1352 (-SO_2-), 1163 (-SO_2-) cm^{-1}; ^{1}H NMR($CDCl_3$ / TFA = 4/1 v/v, 400 MHz) δ: 0.80-1.10 (m, 3H×0.338, C$\underline{H}_3$-$(CH_2)_{11}$S-, 3H, C$\underline{H}_3$-$(CH_2)_3$-N-), 1.10-2.90 (m, 20H×0.338, -(C$\underline{H}_2$)$_{10}$-, 4H, CH_3-(C$\underline{H}_2$)$_2$-CH_2-N-, 2H, -C$\underline{H}_2$-CH-, 1H, -CH_2-C$\underline{H}$-), 2.40-2.60 (m, 3H, C$\underline{H}_3$-CH_4-) 2.90-3.05 (m, 2H×0.338, -S-C$\underline{H}_2$-), 3.05-3.73 (m, 2H, CONH-C$\underline{H}_2$-), 7.30-7.55 (m, 2H, -C$\underline{H}_4$-), 7.70-7.95 (m, 2H, -C$\underline{H}_4$-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.63, 14.07, 22.63, 28.11, 29.31, 29.60, 31.87, 39.46, 41.81, 125.98, 126.10, 128.24, 129.07, 129.54, 135.71, 139.51, 141.03, 141.92, 143.18, 144.83, 151.29, 166.65, 166.76, 173.45, 174.04 ppm.

Hydrolysis of 6a-6b. Polymer **6a** or **6b** was dissolved in 1 *M* NaOH aqueous solution in a round bottomed flask. After the reaction, the

mixture was slightly acidified by 1 *M* HCl aqueous solution and evaporated to dryness. DMF was added to the residue and the insoluble salt was filtrated off. The filtrate was poured into hexane-diethyl ether (6/4 v/v, ca. 100 mL) and the precipitated polymer **7a-7b** was dried *in vacuo*.

Polymer 7a Obtained from 6a at room temperature. Yield 100%, IR (KBr): 3491 (OH), 3238 (NH), 2926, 2855 (CH_3, -CH_2-), 1719 (C=O), 1638 (C=O), 1163 (-SO_2-) cm^{-1}; ^{1}H NMR(DMSO-d_6, 400 MHz) δ: 0.88 (t, J = 6.40 Hz, 3H×0.071, C$\underline{H}_3$-CH_2-), 1.10-1.26 (m, 20H×0.071, -(C$\underline{H}_2$)$_{10}$-), 1.26-1.93 (m, 2H, -C$\underline{H}_2$-CH-), 1.93-2.64 (m, 1H, -CH_2-C$\underline{H}$-), 2.45 (s, 3H×0.5, C$\underline{H}_3$-C_6H_4-), 2.64-2.90 (m, 2H×0.071, -S-C$\underline{H}_2$-), 7.20-7.60 (m, 2H×0.5, -$C_6\underline{H}_4$-), 7.70-8.20 (m, 2H×0.5, -$C_6\underline{H}_4$-) ppm.

Polymer 7a Obtained from 6a at 50°C. Yield 94%, IR (KBr): 3449 (OH), 2928, 2855 (CH_3, -CH_2-), 1718 (C=O), 1638 (C=O) cm^{-1}; ^{1}H NMR(DMSO-d_6, 400 MHz) δ: 0.86 (t, J = 6.40 Hz, 3H×0.071, C$\underline{H}_3$-CH_2-), 1.10-1.26 (m, 20H×0.071, -(C$\underline{H}_2$)$_{10}$-), 1.26-1.93 (m, 2H, -C$\underline{H}_2$-CH-), 1.93-2.64 (m, 1H, -CH_2-C$\underline{H}$-), 2.45 (s, 3H×0.1, C$\underline{H}_3$-C_6H_4-), 2.64-2.90 (m, 2H×0.071, -S-C$\underline{H}_2$-), 7.20-7.60 (m, 2H×0.1, -$C_6\underline{H}_4$-), 7.70-8.20 (m, 2H×0.1, -$C_6\underline{H}_4$-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 13.95, 20.88, 22.07, 27.52, 28.14, 28.69, 29.00, 31.27, 34.69, 41.66, 51.30, 125.60, 125.92, 127.67, 127.04, 128.34, 128.86, 129.28, 172.78, 174.01, 174.89, 176.11 ppm.

Polymer 7b Obtained from 6b at 50°C. Yield 83%, IR (KBr): 3449 (NH, OH), 3246 (NH), 2998, 2928, 2855 (CH_3, -CH_2-), 1701 (C=O), 1663 (C=O), 548 (N-C=O) cm^{-1}; ^{1}H NMR(DMSO-d_6, 400 MHz) δ: 0.80-2.45 (m, 3H×0.243, C$\underline{H}_3$-CH_2-, 3H, -CH_2-C(C$\underline{H}_3$)-, 20H×0.24, -(C$\underline{H}_2$)$_{10}$-, and 2H, -C$\underline{H}_2$-C(CH_3)-), 2.55-2.70 (m, 2H×0.24, -S-C$\underline{H}_2$-), 2.30-2.40 (m, 3H×0.18, C$\underline{H}_3$-C_6H_4-), 7.20-7.60 (m, 2H×0.18, -$C_6\underline{H}_4$-), 7.70-8.20 (m, 2H×0.18, -$C_6\underline{H}_4$-), 10.50 (bs, 1H×0.82, -COO$\underline{H}$) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ:13.99, 16.42, 17.23, 17.85, 18.21, 20.28, 20.94, 22.11, 28.14,

28.71, 28.84, 29.02, 29.30, 31.31, 34.86, 44.20, 44.46, 54.09,125.66, 126.22, 126.57, 127.08, 128.45, 128.91, 129.24, 129.31, 129.50, 177.74, 178.07, 178.86, 179.42 ppm.

Hydrolysis of 6c at 50°C. Polymer **6c** (191.5 mg, 0.17 mmol) was dissolved in 1 *M* NaOH methanol solution (19 mL) in a 100 mL round bottomed flask. After stirring at 50°C for 72 h, 1 *M* HCl aqueous solution (ca. 19 mL) was added and the mixture was evaporated to dryness. To the residue was added chloroform (50 mL) and the resulting chloroform suspension was filtered. The filtrate was evaporated to dryness. The resulting mixture was purified by recycling preparative HPLC (eluent: chloroform) to afford 82 mg of polymer **7c** (78%, 0.13 mmol) and 28 mg of *p*-toluenesulfonamide (99%, 0.16 mmol).

7c. IR (KBr): 3436 (NH), 3299 (NH), 2959, 2924, 2855 (CH_3-, -CH_2-), 1645 (C=O) cm^{-1}; ^{1}H NMR($CDCl_3$, 400 MHz) δ: 0.70-1.03 (m, 3H×0.338, C$\underline{H}_3$-$(CH_2)_{11}$S-, 3H, C$\underline{H}_3$-$(CH_2)_3$-N-), 1.03-2.90 (m, 20H×0.338, -$(C\underline{H}_2)_{10}$-, 4H, CH_3-$(C\underline{H}_2)_2$-CH_2-N-, 2H, -$C\underline{H}_2$-CH-, and 1H, -CH_2-C$\underline{H}$-), 2.37-2.44 (m, 3H×0.1, C$\underline{H}_3$-CH_4-), 2.90-3.05 (m, 2H×0.338, -S-C$\underline{H}_2$-), 3.05-3.75 (m, 2H, CON-C$\underline{H}_2$-), 7.10-7.50 (m, 2H×0.1, -C$\underline{H}_4$-), 7.60-8.10 (m, 2H×0.1, -C$\underline{H}_4$-), 9.13 (bs, 1H×0.9, -N$\underline{H}$) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 13.58, 13.93, 19.94, 21.44, 22.52, 26.54, 26.84, 27.26, 27.81, 28.37, 28.70, 28.83, 29.07, 29.18, 29.52, 29.98, 30.16, 31.34, 31.43, 31.76, 32.05, 32.58, 32.76, 33.27, 33.57, 34.06, 34.61, 34.96, 39.78, 51.56, 128.01, 129.36, 172.22, 173.56, 175.11, 177.22 ppm.

References and Notes

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2) T. Iwamura, I. Tomita, M. Suzuki, and T. Endo, *J. Polym. Sci.: Part A: Polym. Chem.*, in press.

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Chapter 3

Chapter 4

Hydrogen-Transfer Polymerization of Monomers Having Acylsulfonylurea Moieties Derived from *p*-Toluenesulfonyl Isocyanate and Acrylamide Derivatives

Abstract

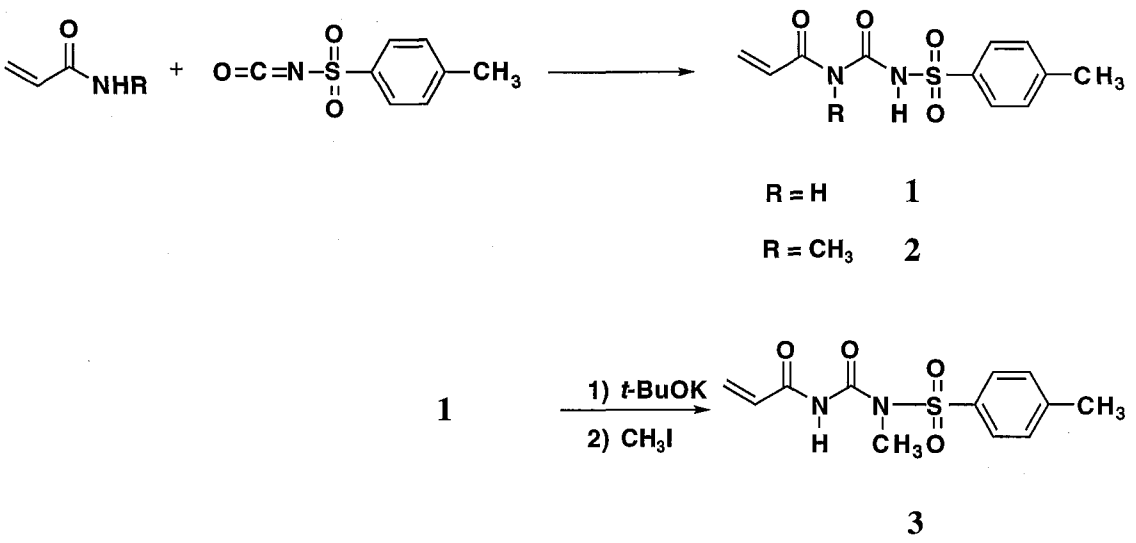
The hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**1**) was carried out at 80°C in *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), acetonitrile (MeCN), or toluene containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical inhibitor for 24 h using *t*-BuOK or 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), (3 mol%) as an initiator. In all cases, polymer **4** was obtained in moderate yield, whose structure was dependent upon the polymerization conditions. That is, the polymer prepared by *t*-BuOK in polar solvents was composed of the hydrogen-transfer polymerization unit selectively, while that by *t*-BuOK in less polar solvents or by DBU was composed of both the hydrogen-transfer and the vinyl polymerization units.

4.1 Introduction

Activated isocyanates such as acyl isocyanate and sulfonyl isocyanate are known to be much more reactive than common isocyanates toward nucleophiles. For example, sulfonyl isocyanates readily react with various nucleophiles such as amides under mild conditions without any catalysts to afford the corresponding adducts. [1-3] Endo *et al.* have developed the synthesis of novel polymers based on *N*-acyl isocyanates and *N*-sulfonyl isocyanates. [4-9] In Chapter 2, the author has described the synthesis of poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) by the radical polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**1**) (i.e., an adduct prepared easily from acrylamide and *p*-toluenesulfonyl isocyanate).[9] The resulting polymer having the -CO-NH-CO-NH-SO_2- repeating unit in the side chain was demonstrated to exhibit a unique hydrolytic character.

Since monomer **1** has two acidic protons on the nitrogen atoms, its anionic polymerization may involve the hydrogen-transfer process as reported previously for acrylamide, methacrylamide, α-substituted acrylamide, β-substituted acrylamide, *N*-substituted acrylamide, etc. [10-14]

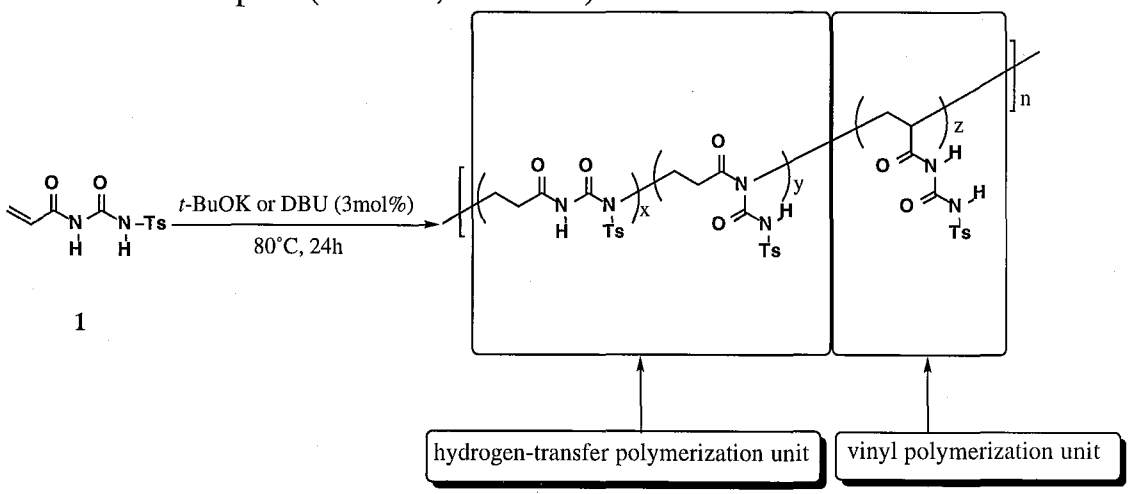
Owing to the characteristics of the hydrogen-transfer polymerization that can incorporate functional groups into the main chain of the polymers, the hydrogen-transfer polymerization of **1** will result in introduction of unique functional groups (i.e., -CO-N(CONHTs)- and/or -CO-NH-CO-N(Ts)-) into the main chain of polymers. Accordingly, detailed results on the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**1**) and its derivatives (**2** and **3**) are described here (Scheme 1).



Scheme 1

4.2 Results and Discussion

Hydrogen-transfer Polymerization of 1. The polymerization of **1** was carried out at 80°C for 24 h using potassium *tert*-butoxide (*t*-BuOK) (3 mol%) as an initiator in various solvents containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical polymerization inhibitor (Scheme 2). As a result, polymer **4** was obtained in the yield of 9-18% as a diethyl ether-insoluble part (Table 1, runs 1-4).



Scheme 2

Table 1. Hydrogen-Transfer Polymerization of *N*-Acryloyl-*N'*-*p*-toluenesulfonylurea (**1**) [a]

Run	Initiator	Solvent	Conv. (%)[b]	Yield (%)[c]	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$)[d]	x / y / z [b]
1	*t*-BuOK	DMF	75	10	4300 (1.07)	52 / 48 / 0
2	*t*-BuOK	DMSO	69	18	3100 (1.38)	61 / 36 / 0
3	*t*-BuOK	MeCN	84	10	5200 (1.13)	32 / 41 / 27
4	*t*-BuOK	PhMe	31	9	3200 (1.20)	3 / 3 / 94
5	DBU	DMF	95	25	3700 (1.37)	36 / 41 / 23
6	DBU	DMSO	89	36	3600 (1.28)	42 / 28 / 30
7	DBU	MeCN	87	26	4300 (1.13)	30 / 39 / 31
8	DBU	PhMe	97	30	3600 (1.11)	30 / 41 / 29

a) Conditions: [**1**] = 1 *M*, initiator (3 mol%), *N*-phenyl-*β*-naphthylamine (1 mol%), 80°C, 24 h.
b) Determined by ^{1}H NMR spectra.
c) Diethyl ether-insoluble part.
d) Estimated by GPC, based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

^{1}H NMR spectra of the obtained polymers suggested that the hydrogen-transfer polymerization proceeded selectively in *N,N*-dimethylformamide (DMF) and dimethylsulfoxide (DMSO) (runs 1 and 2), while both the hydrogen-transfer and the vinyl polymerization took place in acetonitrile (MeCN) and toluene. The ^{1}H NMR spectrum of the polymer obtained in run 1 is shown in Figure 1a, in which two peaks attributable to the methylene protons adjacent to the nitrogen atom and those adjacent to the carbonyl group were observed at δ 3.23 - 4.37 (e, f) and 2.72 - 3.07 (g, h) ppm, respectively. The assignment of the peaks at 7.27-7.98 ppm (b, c) were carried out on the basis of the spectra of model compounds and the ratio of x to y units in Scheme 2 was determined by the integral ratio between these peaks. Because both of two possible hydrogen-transfer units produced through the polymerization, both of the N-H moieties should participate in the hydrogen-transfer process. In the ^{1}H NMR spectrum of the polymer obtained in run 4 (Figure 1b), the signals due to the methylene

protons (e, f, g, h) were small, while those attributable to the methylene protons in the vinyl polymerization unit were observed as major peaks at δ 1.00 - 2.74 (j, k) ppm.

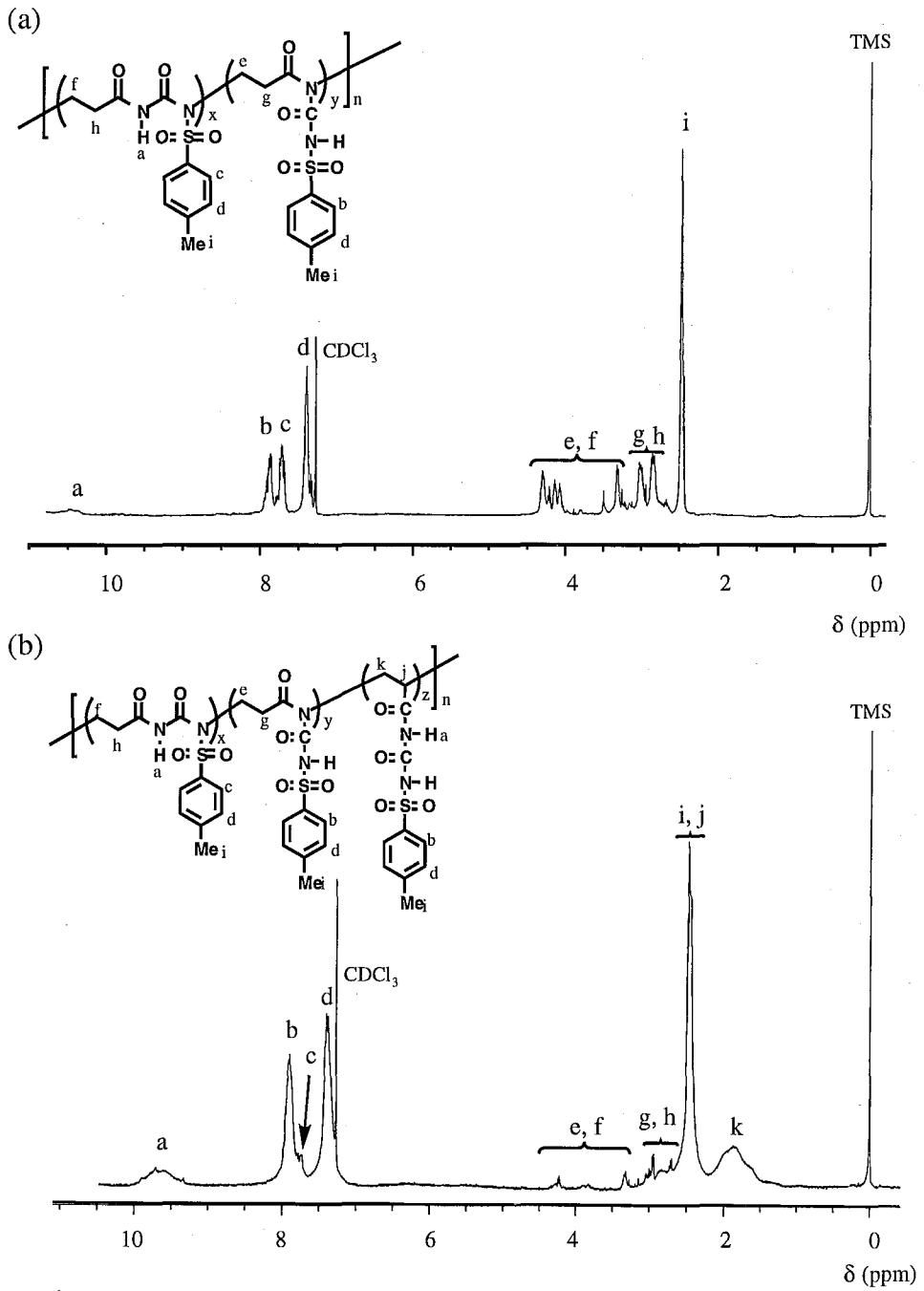
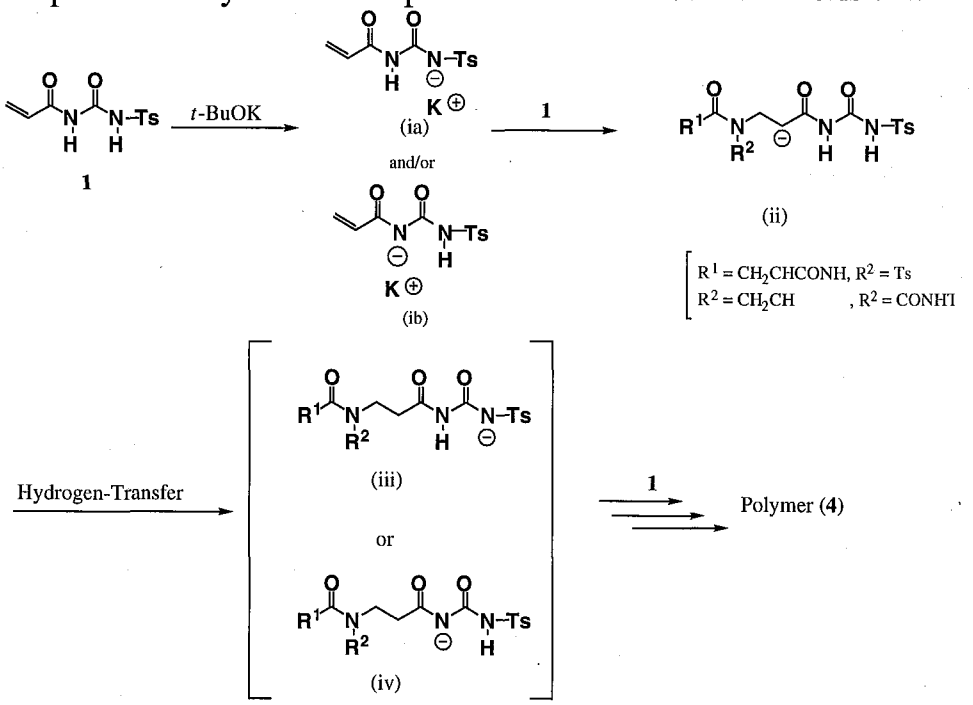


Figure 1 ^{1}H-NMR spectra ($CDCl_3/CF_3COOH$ (v/v=4/1)) of **4** prepared in run 1 (a) and that prepared in run 4 (b).

As the initiation process, two possibilities might be speculated; the nucleophilic addition of the initiating anion (*t*-BuO^-) toward the unsaturated bonds in **1** and the deprotonation of the amidic proton. To clarify this process, **1** was reacted with an equivalent amount of *t*-BuOK at room temperature for 24 h in acetonitrile. The ^{1}H NMR spectrum of the reaction mixture indicated that a potassium salt of **1**, i.e., CH_2=CHCONHCON$^-$TsK$^+$, was produced almost quantitatively as a result of specific deprotonation by *t*-BuOK. When the hydrogen-transfer polymerization of **1** was carried out at 80°C for 24 h using the potassium salt of **1** (3 mol%) as an initiator, a polymer having an identical structure to that prepared by *t*-BuOK was obtained. Therefore, the polymerization is most probably proceeded *via* the potassium salt (ia) and/or (ib) (Scheme 3). In the propagation process, the anion (ii) generated by the nucleophilic attack at the β-carbon atom of **1** may give rise to two kinds of *N*-anions ((iii) and (iv)) through the hydrogen-transfer process. The hydrogen-transfer polymerization units should be produced by the nucleophilic attack of these *N*-anions toward **1**.



Scheme 3

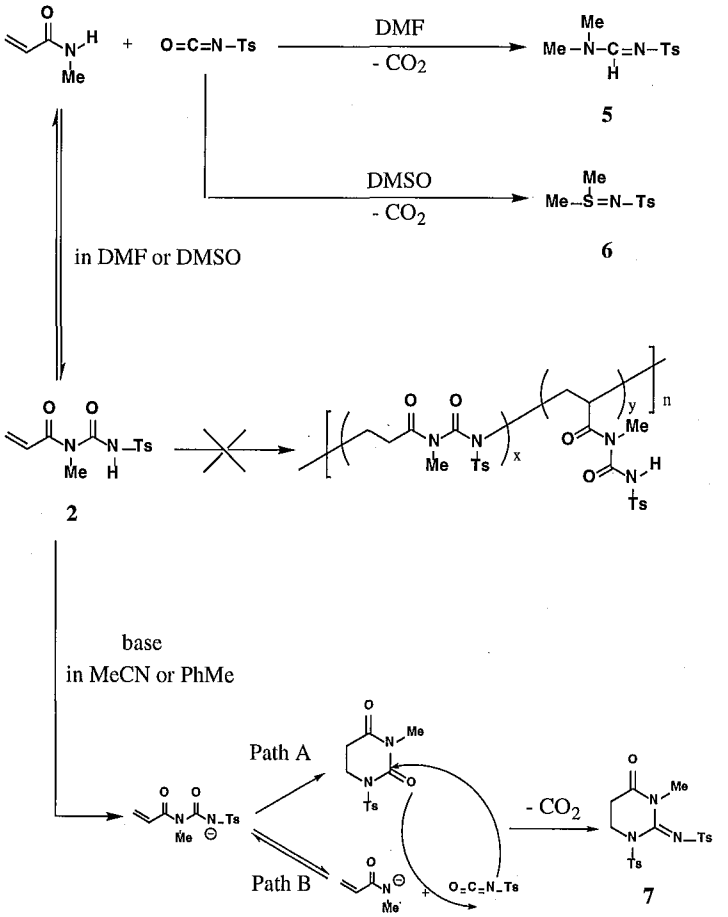
When 1,8-Diazabicyclo[5,4,0]undec-7-ene (DBU) (3 mol%) was used as an initiator for the polymerization of **1**, monomer **1** was highly converted irrespective of the solvents under the same conditions to the case of *t*-BuOK and polymer **4** ($\overline{M}_n$ = 3700-4300) was obtained in a better yield as a diethyl ether-insoluble part (Table 1, runs 5-8). From the structural elucidation of polymer **4** by ^{1}H NMR spectra, all the polymers produced were revealed to possess both the hydrogen-transfer and the vinyl polymerization units whose ratio seemed not to be effected by the solvents used for the polymerization.[15]

Hydrogen-transfer Polymerization of 2 and 3. The monomers having either one of the two active hydrogens (**2** and **3**) were subjected to the polymerization under the same conditions. In the case of *N*-acryloyl-*N*-methyl-*N'*-*p*-toluenesulfonylurea (**2**), the diethyl ether-insoluble products were obtained, which were, however, low molecular-weight compounds (Table 2). From the detailed analyses of the products, their structures were found to be dependent on the solvents used for the reaction. In DMF, a single product was obtained as a diethyl ether-insoluble part which was identified as *N,N*-dimethyl-*N'*-*p*-toluenesulfonyl formamidine (**5**) by comparing the melting point and the FAB/MS spectrum with those of the authentic sample (runs 1 and 6).[16] In DMSO, a compound identified as *N*-*p*-toluenesulfonyl dimethyl sulfimine (**6**) [16] was obtained in 57 or 59% yield (runs 2 and 7). In MeCN or toluene, a product was identified as **7** by the FAB/MS spectra (m/z 436 $[M+H]^+$) as well as ^{1}H and ^{13}C NMR spectra (runs 3-5, 8, and 9).[17] The formation of these products (**5**-**7**) rather than the polymer from monomer **2** might be explained by assuming the decomposition of **2** into *p*-toluenesulfonyl isocyanate and *N*-methylacrylamide (Scheme 4). It is known that sulfonyl isocyanates react easily with amides and sulfoxides thorough the elimination of CO_2.[16]

Table 2 Low Molecular-Weight Products from *N*-Acryloyl-*N*-methyl-*N'*-*p*-toluenesulfonylurea (**2**)[a].

Run	Initiator	Solvent	R_f[b]	$[M + H]^+$[c]	Product	Yield (%)[d]
1	*t*-BuOK	DMF	0.5	227	**5**	44
2	*t*-BuOK	DMSO	0.3	232	**6**	55
3	*t*-BuOK	MeCN	0.9	436	**7**	57
4	*t*-BuOK	MeCN	0.9	436	**7**	87[e]
5	*t*-BuOK	PhMe	0.9	436	**7**	36
6	DBU	DMF	0.5	227	**5**	42
7	DBU	DMSO	0.3	232	**6**	59
8	DBU	MeCN	0.9	436	**7**	48
9	DBU	PhMe	0.9	436	**7**	32

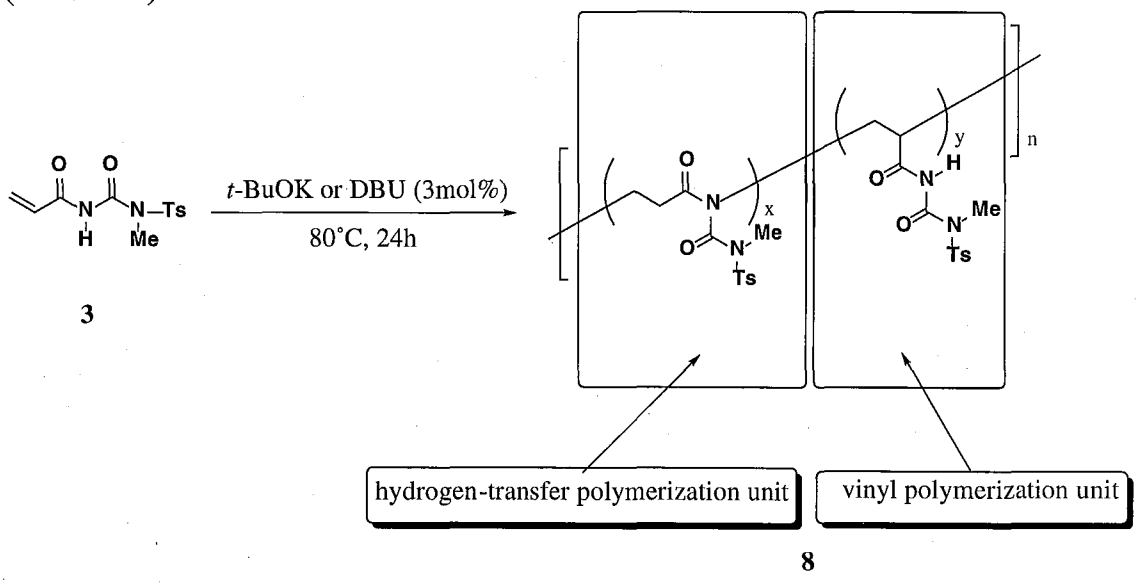
a) Conditions: [**2**] = 1 *M*, initiator (3 mol%), *N*-phenyl-*β*-naphthylamine (1 mol%), 80°C, 24 h.
b) TLC (eluent: chloroform / methanol 9/1 v/v).
c) A matrix for FAB/MS: *m*-nitrobenzyl alcohol.
d) Diethyl ether-insoluble part.
e) Isolated yield by silica gel column chromatography (eluent: chloroform / methanol 9/1 v/v).



Scheme 4

Thus, the products (**5** and **6**) obtained in DMF and DMSO, respectively, might be regarded as the adducts of the isocyanate with the solvents. When the reaction was carried out in less nucleophilic solvents such as toluene or MeCN, the product (**7**) might be produced by the base-catalyzed intramolecular conjugate addition of **2** and the subsequent condensation with the isocyanate.

The hydrogen-transfer polymerization of *N*-acryloyl-*N'*-methyl-*N'*-*p*-toluenesulfonylurea (**3**) was carried out under the same conditions. In this case, polymer **8** was obtained in moderate yields as a diethyl ether-insoluble product (Scheme 5 and Table 3). From the structural elucidation, the polymer obtained by using *t*-BuOK as an initiator was found to be composed of the specific hydrogen-transfer unit irrespective of the solvents (runs 1-4).



3 **8**

Scheme 5

In Figure 2, the ^{1}H-NMR spectrum of the polymer obtained in run 3 is shown as a typical example. No methylene protons attributable to the vinyl polymerized structure was observed at δ 1.00 - 2.74 ppm, while those adjacent to the nitrogen were observed at δ 3.60 - 4.50 ppm as a result of the hydrogen-transfer process. By using DBU (3 mol%), the polymerization

proceeded both by the hydrogen-transfer and the vinyl polymerization, whose ratio was determined as x : y = 55 : 45 - 67 : 33 (runs 5-8).[18)]

Table 3 Hydrogen-Transfer Polymerization of *N*-Acryloyl-*N'*-methyl-*N'*-*p*-toluenesulfonylurea (**3**).

Run	Initiator	Solvent	Conv. (%)[b)]	Yield (%)[c)]	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$)[d)]	x / y [b)]
1	*t*-BuOK	DMF	75	11	7200 (1.51)	100 / 0
2	*t*-BuOK	DMSO	69	19	5300 (1.86)	100 / 0
3	*t*-BuOK	MeCN	84	33	8600 (1.42)	100 / 0
4	*t*-BuOK	PhMe	85	14	9600 (1.75)	100 / 0
5	DBU	DMF	68	14	9900 (1.39)	55 / 45
6	DBU	DMSO	97	22	8200 (1.25)	56 / 44
7	DBU	MeCN	76	28	7700 (1.41)	67 / 33
8	DBU	PhMe	74	21	7900 (2.09)	61 / 39

a) Conditions: [**3**] = 1 *M*, initiator (3 mol%), *N*-phenyl-*β*-naphthylamine (1 mol%), 80°C, 24 h.
b) Determined by ^{1}H NMR spectra.
c) Diethyl ether-insoluble part.
d) Estimated by GPC, based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

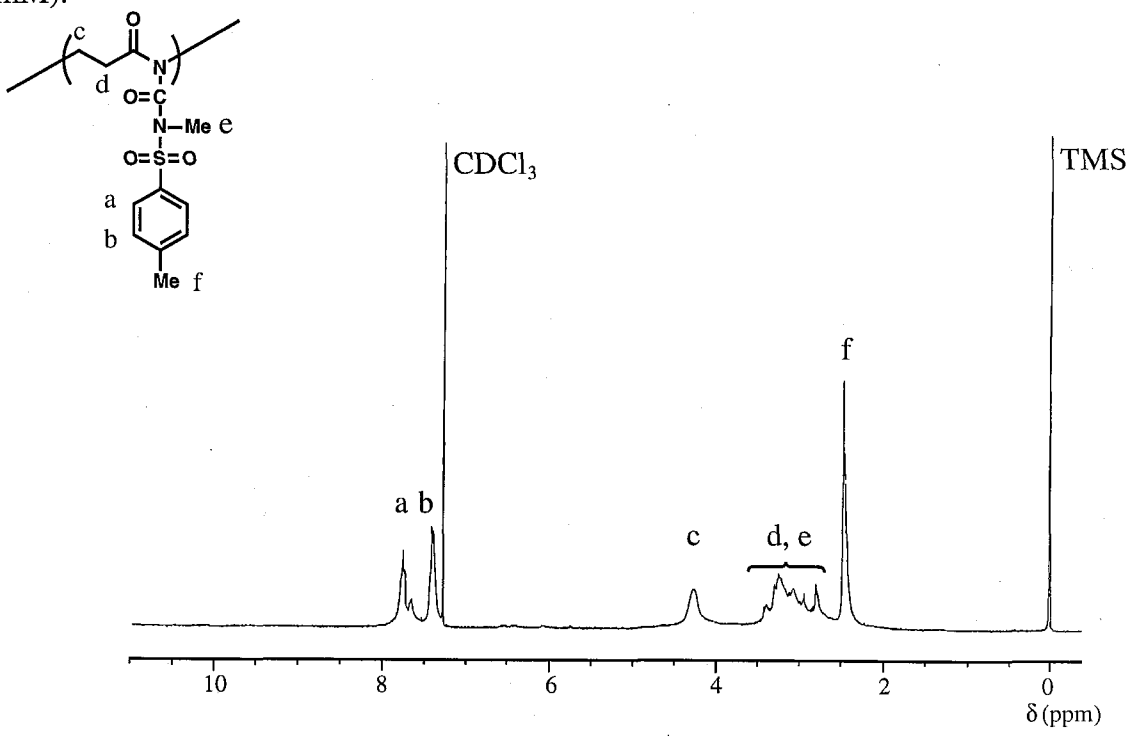


Figure 2 ^{1}H-NMR spectrum of **8** ($CDCl_3/CF_3COOH$ (v/v=4/1)).

4.3 Experimental

Materials. 1,8-Diazabicyclo[5,4,0]undec-7-ene (DBU), *N,N*-dimethylformamide (DMF), dimethylsulfoxide (DMSO), and acetonitrile (MeCN) were dried over CaH_2, distilled, and stored under nitrogen. Toluene was dried over sodium metal and distilled under nitrogen. Potassium *tert*-butoxide (*t*-BuOK) was prepared from *t*-butanol and potassium. *N*-Acryloyl-*N'*-*p*-toluenesulfonylurea (**1**) was prepared the procedure by described in Chapter 2.[9] Other commercially available reagents were used without further purification.

Measurements. IR spectra were measured on a JASCO FT/IR-5300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-EX90 (^{1}H NMR: 90 MHz, ^{13}C NMR: 22.4 MHz) or JEOL JNM-EX400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) spectrometer.

Number- ($\overline{M}_n$) and weight-average ($\overline{M}_w$) molecular weights and molecular weight distributions ($\overline{M}_w/\overline{M}_n$) were estimated by gel permiation chromatography (GPC) on a Tosoh Co. HLC-8020 system equipped with polystyrene gel columns (TSK® gel G6000HXL, TSK® gel G5000HXL, TSK® gel G4000HXL and TSK® gel G2500HXL) using DMF containing LiBr (5.8 mM) as eluent, a flow rate of 1.0 mL/min, polystyrene calibration, and an ultraviolet (UV) detector.

Fast atom bombardment mass spectra (FAB/MS) were recorded by using a JEOL JMS-700 spectrometer, whereby a mixture of a sample and *m*-nitrobenzyl alcohol on a standard FAB target was subjected to a beam of xenon atoms produced at 6 keV, 2 mA.

Synthesis of *N*-Acryloyl-*N*-methyl-*N'*-*p*-toluenesulfonyl urea (2). To a 20 mL round-bottomed flask containing a benzene (8 mL) solution of *p*-toluenesulfonyl isocyanate (1.40 g, 7.09 mmol) was added

N-methylacrylamide (0.59 g, 6.88 mmol). The mixture was stirred at room temperature for 29 h, and subsequently heated at 40°C for 4 h under nitrogen. The resulting mixture was evaporated to dryness and the residue was purified by chromatography on silica gel with chloroform as eluent to isolate the *N*-methylated monomer **2**, which was further purified by recrystallization from benzene. Yield 87% (1.69 g, 5.99 mmol), mp. 110.0-110.5°C. IR (KBr) 3414 (NH), 1715 (C=O), 1664 (C=O), 1618 (C=C), 1449 (-CH_2-), 1358 (-SO_2-), 1175 (-SO_2-), 548 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ: 2.44 (s, 3H, $C\underline{H}_3$- C_6H_4-), 3.26 (s, 3H, $C\underline{H}_3$-N-), 5.97 (dd, *J*=7.61 and 4.32 Hz, 1H, CH_2=C$\underline{H}$-), 6.58 (d, *J*=4.32 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 6.60 (d, *J*=7.61 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 7.33 (d, *J*=8.37 Hz, 2H, $C_6\underline{H}_4$), 7.98 (d, *J*=8.37 Hz, 2H, $C_6\underline{H}_4$), 12.11 (bs, 1H, -CON$\underline{H}$$SO_2$-) ppm; ^{13}C NMR (DMSO-d_6, 22.4 MHz), δ: 21.2, 31.2, 127.5, 128.7, 129.5, 133.8, 135.9, 144.8, 150.1, 170.0 ppm; ANAL. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.05%; H, 5.00%; N, 9.92%; S, 11.36%. Found: C, 50.99%; H, 4.96%; N, 9.87%; S, 11.30%.

Synthesis of *N*-Acryloyl-*N'*-methyl-*N'*-*p*-toluenesulfonyl urea (3). To a 100 mL round bottomed flask containing a DMF (20 mL) solution of *t*-BuOK (2.03 g, 18.09 mmol) and *N*-phenyl-β–naphthylamine (65.4 mg, 0.30 mmol) was added *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**1**, 5.27 g, 19.64 mol) under nitrogen. After the mixture was stirred at room temperature for 15 h, methyl iodide (5.68 g, 40.02 mmol) was added and the mixture was stirred at ambient temperature for 5 days. The resulting mixture was treated with water and extracted with chloroform. The organic phase was washed with water three times, dried over $MgSO_4$, and evaporated to dryness. The residue was purified by chromatography on silica gel with chloroform as eluent to isolate the *N'*-methylated monomer **3**, which was further purified by recrystallization from hexane-chloroform.

Yield 45% (2.48 g, 8.78 mmol), mp. 85-86°C. IR (KBr) 3410 (NH), 3113 (C=C), 1725 (C=O), 1694 (C=O), 1630 (C=C), 1460 (-CH_2-), 1356 (-SO_2-), 1152 (-SO_2-), 546 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ: 2.46 (s, 3H, $C\underline{H}_3$-C_6H_4-), 3.16 (s, 3H, $C\underline{H}_3$-N-), 5.89 (dd, J = 9.60 and 2.00 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 6.46 (dd, J = 19.60 and 2.00 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 6.80 (dd, J = 19.60 and 9.60 Hz, 1 H, CH_2=C$\underline{H}$-), 7.37 (d, J = 8.30 Hz, 2H, $C_6\underline{H}_4$), 7.74 (d, J = 8.30 Hz, 2H, $C_6\underline{H}_4$), 10.13 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 22.4 MHz), δ: 21.6, 32.4, 127.1, 129.9, 130.4, 131.0, 134.3, 145.9, 148.8, 164.7 ppm; ANAL. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.05%; H, 5.00%; N, 9.92%; S, 11.36%. Found: C, 50.99%; H, 4.96%; N, 9.86%; S, 11.12%.

Synthesis of Potassium Salt of 1. To a 100 mL round bottomed flask containing a acetonitrile (20 mL) solution of *t*-BuOK (0.21 g, 1.87 mmol) was added *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (**1**, 0.50 g, 1.86 mmol) under nitrogen. After the mixture was stirred at room temperature for 24 h, the resulting suspension was evaporated to dryness to give essentially pure form of the potassium salt. IR (KBr) 3451 (NH), 1716 (C=O), 1664 (C=O), 1624 (C=C), 1321 (-SO_2-), 1142 (-SO_2-), 556 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.46 (s, 3H, $C\underline{H}_3$- C_6H_4-), 5.89 (d, J=10.80 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 6.49 (d, J=17.20 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 6.76 (dd, J=10.80 and 17.20 Hz, 1H, CH_2=C$\underline{H}$-), 7.38 (d, J=8.00 Hz, 2H, $C_6\underline{H}_4$), 7.73 (d, J=8.00 Hz, 2H, $C_6\underline{H}_4$), 10.14 (s, 1H, -CON$\underline{H}$CO-) ppm.

Hydrogen-transfer Polymerization (Typical Procedure). Monomer (**1**, **2**, or **3**) (1.0 *M*), *t*-BuOK or DBU (3 mol%), and *N*-phenyl-β–naphthylamine (1 mol%, an inhibitor for radical polymerization) were dissolved in DMF, DMSO, MeCN or toluene in a test tube under nitrogen atmosphere. After heating at 80°C for 24 h, the resulting mixture was poured into diethyl ether and the isolated polymer was dried *in vacuo*.

Polymer 4 Obtained from 1 (Run 1 in Table 1). Yield 10%; IR (KBr) 3436 (NH), 2924 (-CH_2-), 2855 (-CH_2-), 1769 (C=O), 1692 (C=O), 1476 (-CH_2-), 1383 (-SO_2-), 1159 (-SO_2-), 766 (-CH_2-), 550 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.46 (s, 3H×0.9, C$\underline{H}_3$-C_6H_4-), 2.72-3.07 (m, 2H, -CH_2-C$\underline{H}_2$-CO-), 3.23-4.37 (m, 2H, -N-C$\underline{H}_2$-CH_2-), 7.27-7.48 (m, 2H×0.9, CH_3-$C_6\underline{H}_4$-), 7.60-7.80 (m, 2H×0.47, -$C_6\underline{H}_4$-SO_2- in x unit), 7.80-7.97 (m, 2H×0.43, -$C_6\underline{H}_4$-SO_2- in y unit), 10.48 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.0, 30.9, 31.4, 34.8, 35.9, 36.8, 37.7, 40.7, 125.5, 126.5, 128.0, 129.6, 135.3, 137.3, 142.7, 144.8, 145.8, 148.6, 149.6, 150.0, 168.9, 172.8 ppm.

Polymer 4 Obtained from 1 (Run 4 in Table 1). Yield 9%; IR (KBr) 3449 (NH), 2928 (-CH_2-), 2857 (-CH_2-), 1769 (C=O), 1701 (C=O), 1451 (-CH_2-), 1352 (-SO_2-), 1161 (-SO_2-), 764 (-CH_2-), 550 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.00-2.74 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$-), 2.46 (s, 3H×0.94, C$\underline{H}_3$-C_6H_4-), 2.72-3.07 (m, 2H×0.07, -CH_2-C$\underline{H}_2$-CO-), 3.23-4.37 (m, 2H×0.07, -N-C$\underline{H}_2$-CH_2-), 7.00-7.64 (m, 2H, CH_3-$C_6\underline{H}_4$-), 7.64-7.82 (m, 2H×0.03, -$C_6\underline{H}_4$-SO_2- in x unit), 7.70-8.20 (m, 2H×0.97, -$C_6\underline{H}_4$-SO_2- in y and z unit), 9.70 (bs, 1H×0.55H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.0, 30.9, 33.8, 34.9, 36.0, 44.7, 125.6, 126.5, 127.7, 129.3, 135.3, 137.2, 141.3, 141.9, 144.6, 167.8, 170.3 ppm.

Low Molecular-Weight Product Obtained from 1. The diethyl ether-soluble part (30%) was characterized as follows; IR (KBr) 3200 (NH), 1716 (C=O), 1381 (-SO_2-), 1186 (-SO_2-), 547 (N-C=O) cm^{-1}; ^{1}H NMR (DMSO-d_6, 90 MHz) δ: 2.41 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.75 (t, J = 6.50 Hz, 2H, -CH_2-C$\underline{H}_2$-CO-), 4.03 (t, J = 6.50 Hz, 2H, -N-C$\underline{H}_2$-CH_2-), 7.43 (d, J = 8.28 Hz, 2H, $C_6\underline{H}_4$), 7.87 (d, J = 8.28 Hz, 2H, $C_6\underline{H}_4$), 10.79 (s, 1H, -CON$\underline{H}$CO-)ppm.; ^{13}C NMR (DMSO-d_6, 22.4 MHz) δ: 21.0, 40.8, 128.0, 129.5, 135.4, 144.7, 149.7, 170.1 ppm.

Low Molecular-Weight Compound (5) Obtained from 2 in DMF (Run 1 in Table 2). Yield 44%; R_f = 0.5 (chloroform / methanol 9/1 v/v); IR (KBr) 1626 (-C=N-), 1346 ($-SO_2-$), 1142 ($-SO_2-$) cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ: 2.46 (s, 3H, $C\underline{H}_3-C_6H_4-$), 3.23 (s, 3H, $C\underline{H}_3-N-$), 3.48 (s, 3H, $C\underline{H}_3-N-$), 7.40 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 7.75 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 8.34 (s, 1H) ppm; ^{13}C NMR (100MHz, $CDCl_3$) δ: 21.3, 35.3, 41.3, 126.3, 129.2, 139.5, 142.3, 159.0 ppm; FAB/MS *m/z* 227 $[M+H]^+$.

Low Molecular-Weight Compound (6) Obtained from 2 in DMSO (Run 2 in Table 2). Yield 55%; R_f = 0.3 (chloroform / methanol v/v = 9/1); IR (KBr) 1273 ($-SO_2-N-$), 1136 ($-SO_2-$) cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ: 2.47 (s, 3H, $C\underline{H}_3-C_6H_4-$), 3.17 (s, 6H, $C\underline{H}_3-S-$), 7.42 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 7.79 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$) ppm; ^{13}C NMR (100MHz, $CDCl_3$) δ: 21.2, 35.7, 126.0, 129.2, 141.1, 141.7 ppm; FAB/MS *m/z* 232 $[M+H]^+$.

Low Molecular-Weight Compound (7) Obtained from 2 in Acetonitrile (Run 4 in Table 2). Yield 87%; R_f = 0.9 (chloroform / methanol 9/1 v/v); IR (KBr) 1726 (C=O), 1595 (-C=N-), 1381 ($-SO_2-$), 1142 ($-SO_2-$) cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ: 2.45 (s, 3H, $C\underline{H}_3-C_6H_4-$), 2.47 (s, 3H, $C\underline{H}_3-C_6H_4-$), 3.12 (s, 3H, $C\underline{H}_3-N-$), 3.57 (t, *J*=6.40 Hz, 2H, $-CH_2-C\underline{H}_2-CO-$), 4.12 (t, *J*=6.40 Hz, 2H, $-N-C\underline{H}_2-CH_2-$), 7.36 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 7.39 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 7.80 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$), 7.89 (d, *J*=8.40 Hz, 2H, $-C_6\underline{H}_4-$) ppm; ^{13}C NMR (100MHz, $CDCl_3$) δ: 21.5, 21.6, 28.6, 30.5, 39.3, 126.6, 128.7, 129.5, 129.6, 134.8, 138.5, 143.6, 145.6, 149.4, 164.2 ppm; FAB/MS *m/z* 436 $[M+H]^+$.

Polymer 8 Obtained from 3 (Run 3 in Table 3). IR (KBr) 3449 (NH), 2961 ($-CH_2-$), 2926 ($-CH_2-$), 1746 (C=O), 1701 (C=O), 1458 ($-CH_2-$), 1366 ($-SO_2-$), 1165 ($-SO_2-$), 756 ($-CH_2-$), 548 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.46 (s, 3H, $C\underline{H}_3-C_6H_4-$), 2.55-3.55 (m, 5H, -

N-C$\underline{H}_3$, and -CH_2-C$\underline{H}_2$-CO-), 3.60-4.50 (m, 2H, -N-C$\underline{H}_2$-CH_2-), 7.27-7.50 (m, 2H, CH_3-$C_6\underline{H}_4$-), 7.50-7.90 (m, 2H, -$C_6\underline{H}_4$-SO_2-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.0, 32.8, 34.3, 37.8, 45.3, 46.8, 126.7, 127.3, 128.3, 129.7, 130.4, 133.8, 136.2, 142.6, 143.4, 146.0, 164.5, 171.6 ppm.

Low Molecular-Weight Product Obtained from 3. Yield 43%; IR (KBr) 3275 (NH), 2984 (CH_3), 2928 (CH_3), 1319 (-SO_2-), 1157 (-SO_2-), 551 (N-C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ: 2.43 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.63 (d, J= 2.70 Hz, 3H, -N-C$\underline{H}_3$), 4.83 (bs, 1H, -N$\underline{H}$-), 7.31 (d, J = 8.19 Hz, 2H, $C_6\underline{H}_4$), 7.76 (d, J = 8.19 Hz, 2H, $C_6\underline{H}_4$) ppm.; ^{13}C NMR ($CDCl_3$, 22.4 MHz) δ: 21.4, 29.2, 127.2, 129.7, 135.7, 143.4 ppm.

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15) The peak area of the aromatic protons were smaller than expected (Table 1: runs 1-4, by 0-22%; runs 5-8, by 35-57%). However, low molecular-weight compounds consisted of the eliminated aromatic parts from the monomer or the polymer were not detected in the diethyl ether-soluble part, while a 6-membered cyclic compound (i.e., intramolecular 1,4-conjugate adduct) was isolated in 30% yield (Table 1, run 8).

16) C. King, *J. Org. Chem.*, **25**, 352 (1960).

17) In the ^{13}C NMR spectrum of **7**, a signal due to a carbonyl group was observed at δ149.4 ppm which is close to the chemical shift of the signal due to the carbonyl group of the *N*-methyl amide moieties (δ 150.1 ppm) rather than that of the urea group (δ 170.0 ppm) in **3**. Thus, product **7** may have a structure as illustrated in Scheme 4.

18) As noted in ref. (15), the peak area of the aromatic protons observed in the ^{1}H NMR spectrum of polymer **8** was also smaller than those expected from the peak intensities of the protons of the main chain (Table 3: runs 1-4, by 0-10%; runs 5-8, by 39-71%). In this case, the eliminated *N*-methyl-*p*-toluenesulfonamide was isolated from the diethyl ether-soluble part (43% yield in run 5). This fact indicates that side reactions accompanying the elimination of *N*-methyl-*p*-toluenesulfonamide from the side chain of the vinyl polymerization unit of polymer **8** also take place under the polymerization conditions.

Chapter 5

Hydrogen-Transfer Polymerization of Vinyl Monomers Having Diacylura Moieties Derived from 4-Methylbenzoyl Isocyanate and Acrylamide Derivatives

Abstract

The anionic polymerization of *N*-acryloyl-*N'*-(4-methylbenzoyl)urea (**1**) was carried out at 80°C for 24 h in DMF, DMSO, acetonitrile or toluene by *t*-BuOK or DBU (3 mol%) as an initiator to obtain polymer **3** in a good yield. The structure of **3** was dependent upon the initiator used, in which *t*-BuOK selectively conducted the hydrogen-transfer polymerization, while DBU partially induced the vinyl polymerization (16-20%).

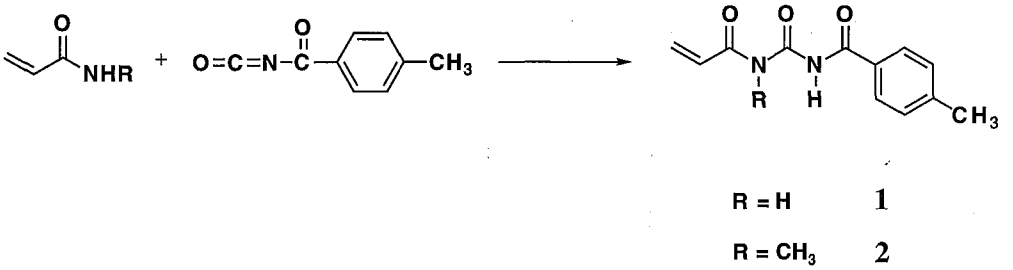
5.1 Introduction

Acyl isocyanate is known to be much more reactive than common isocyanates toward nucleophiles. For example, acyl isocyanates readily react with weak nucleophiles such as amides under mild conditions without any catalysts to afford the corresponding adducts.[1-3] Endo *et al.* have developed the synthesis of novel polymers based on *N*-acyl isocyanates.[4-8] For instance, poly(*N,N'*-diacylurea) having -CO-NH-CO- groups in the main chain have been prepared by the polyaddition of bifunctional acyl isocyanate and diamide.[5] Poly(*N*-acryloyl-*N'*-benzoylurea) bearing the -CO-NH-CO- groups in the side chains have been also prepared by the radical polymerization of *N*-acryloyl-*N'*-benzoylurea (i.e., an adduct prepared easily from acrylamide and benzoyl isocyanate).[6]

In Chapter 4, the author has described the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea prepared by the reaction of *p*-toluenesulfonyl isocyanate and acrylamide.[9] Since the monomer having *N*-acyl-*N'*-sulfonylurea moiety has two acidic protons on the nitrogen atoms, its anionic polymerization involves the hydrogen-transfer process as reported previously for acrylamide, methacrylamide, α-substituted acrylamide, β-substituted acrylamide, *N*-substituted acrylamide, etc. [10-14] Owing to the characteristics of the hydrogen-transfer polymerization, functional groups such as -CO-N($CONHSO_2R$)- and -CO-NH-CO-N(SO_2R)- can be incorporated into the main chains of the polymers.

N-Acryloyl-*N'*-(4-methylbenzoyl)urea (**1**) (i.e., a derivative of *N,N'*-diacylureas) has also two amide protons on the nitrogen atoms whose difference in acidity may exert an interesting influence on the

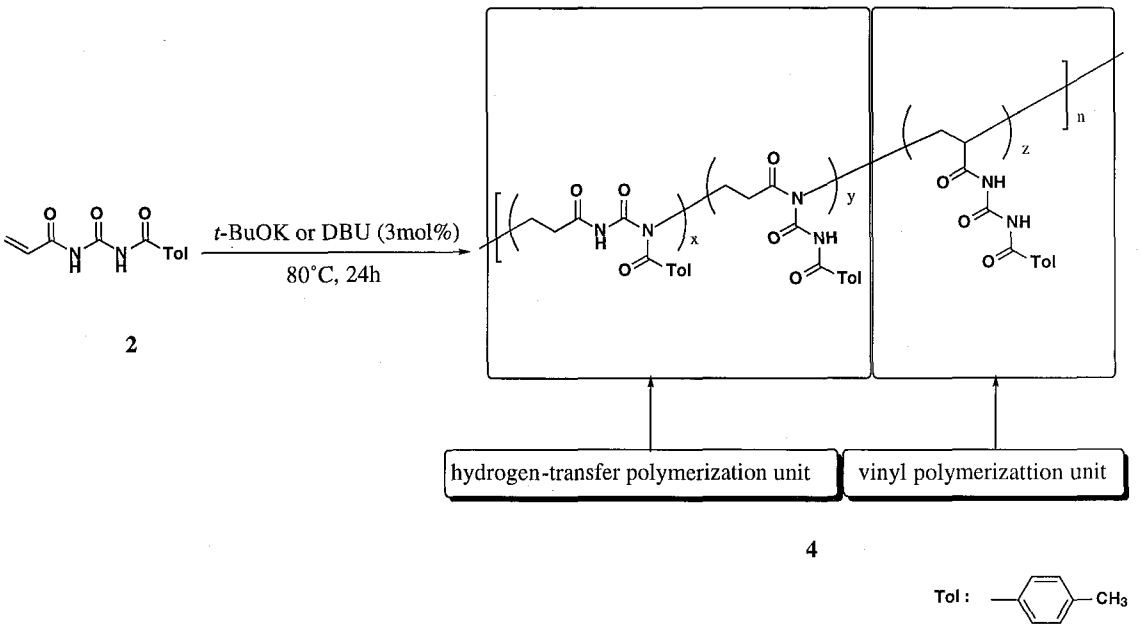
hydrogen-transfer polymerization behavior. The polymerization of monomer **1** will result in introduction of unique functional groups (i.e., -CO-N(CONHCOR)- or -CO-NH-CO-N(COR)-) into the main chain of the polymers which may be of importance for new functional polymers. In this Chapter, the author describes detailed results on the hydrogen-transfer polymerization of **1**. Additionally, the anionic polymerization behavior of monomer **2** having one NH group is also described.



Scheme 1

5.2 Results and Discussion

Hydrogen-Transfer Polymerization of 1. The polymerization of **1** was carried out at 80°C for 24 h using potassium *tert*-butoxide (*t*-BuOK) (3 mol%) as an initiator in various solvents containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical polymerization inhibitor to obtain polymer **3** in 40-60 % yield as a diethyl ether-insoluble part (Scheme 2, Table 1, runs 1-4). From the ^{1}H NMR spectra of all the polymers obtained, the hydrogen-transfer polymerization was found to proceed exclusively irrespective of the solvents. 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 3.60 - 4.50 (d, f) and 2.60 - 3.55 (e, g) ppm, respectively.



Scheme 2

Table 1. Hydrogen-Transfer Polymerization of *N*-Acryloyl-*N'*-4-methylbenzoylurea (**1**)[a)]

Run	Initiator	Solvent	Conv. (%)[b)]	Yield (%)[c)]	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$)[d)]	x / y / z [b)]
1	*t*-BuOK	DMF	100	46	4900 (1.22)	37 / 63 / 0
2	*t*-BuOK	DMSO	100	60	4500 (1.33)	32 / 68 / 0
3	*t*-BuOK	MeCN	100	40	5200 (1.30)	41 / 59 / 0
4	*t*-BuOK	PhMe	100	52	7300 (1.69)	78 / 22 / 0
5	DBU	DMF	100	54	4400 (1.23)	32 / 50 / 18
6	DBU	DMSO	100	62	4100 (1.21)	27 / 57 / 16
7	DBU	MeCN	100	50	4600 (1.31)	31 / 49 / 20
8	DBU	PhMe	100	56	6100 (2.41)	50 / 30 / 20

a) Conditions: [**1**] = 1 *M*, initiator (3 mol%), inhibitor : *N*-phenyl-*β*-naphthylamine (1 mol%), 80°C, 24h.
b) The ratio of x, y to z in Scheme 2, determined by ^{1}H NMR spectra.
c) Diethyl ether-insoluble part.
d) Estimated by GPC based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

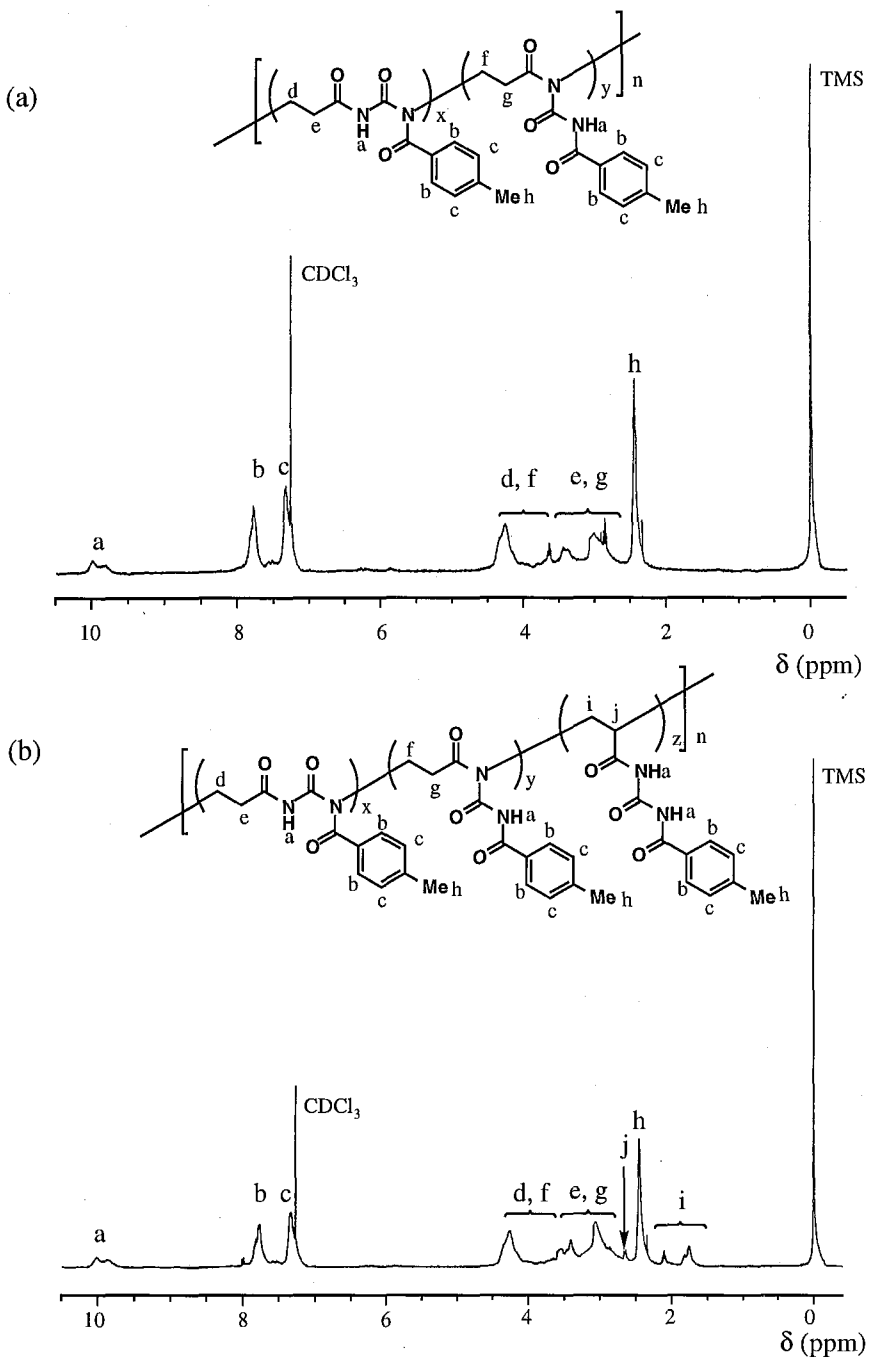
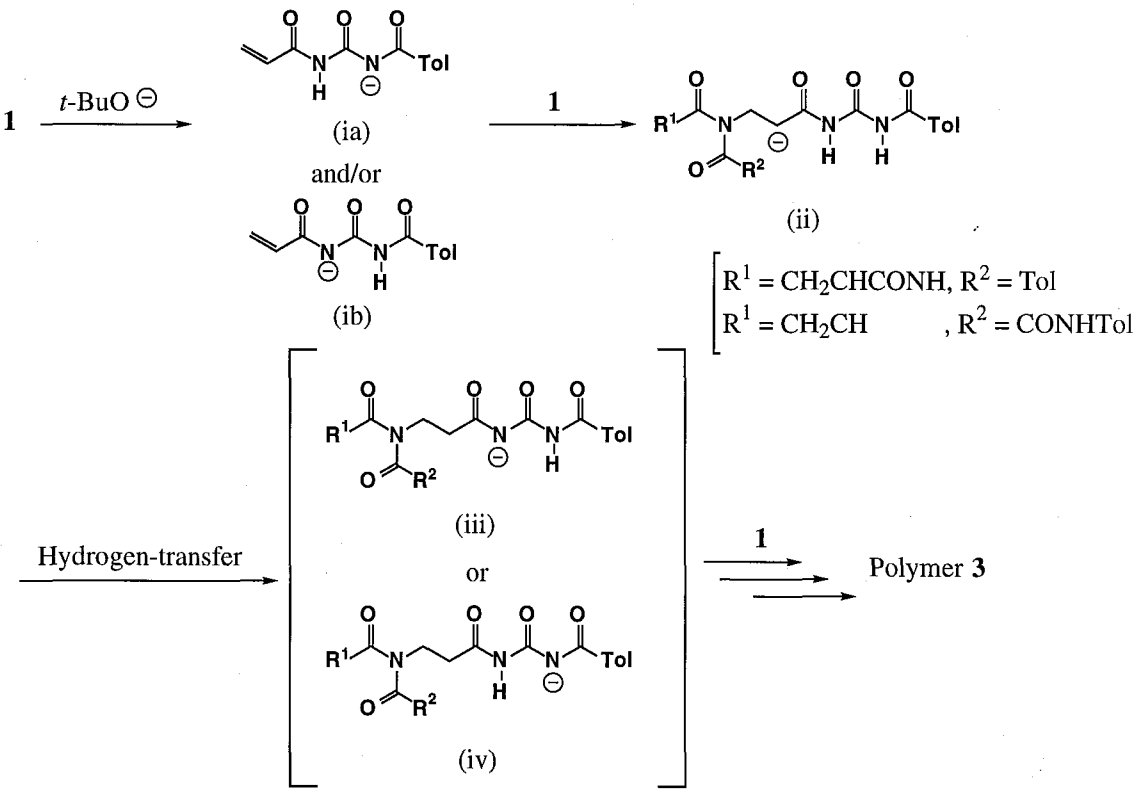


Figure 1 ^{1}H-NMR spectra (in $CDCl_3/CF_3COOH$, v/v=4/1) of **3** prepared in run 1 (a) and that prepared in run 5 (b).

Scheme 3 shows the process of the polymerization. On the initiation step, *N*-anions (ia) or (ib) might be generated from monomer **1** by *t*-BuOK.[17] The anion (ii) generated by the nucleophilic attack to the *β*-carbon atom of **1** may be transformed to two kinds of *N*-anions (iii) and

(iv) through the hydrogen-transfer from two different amide protons in the propagation step. The nucleophilic attack of these *N*-anions toward **1** produces two types of amide units in the main chain of the polymer. The ratio of these unit, (x : y) was determined by the integral ratio of the residual amide protons observed at 9.0-10.0 ppm in ^{1}H NMR spectra (Table 1).

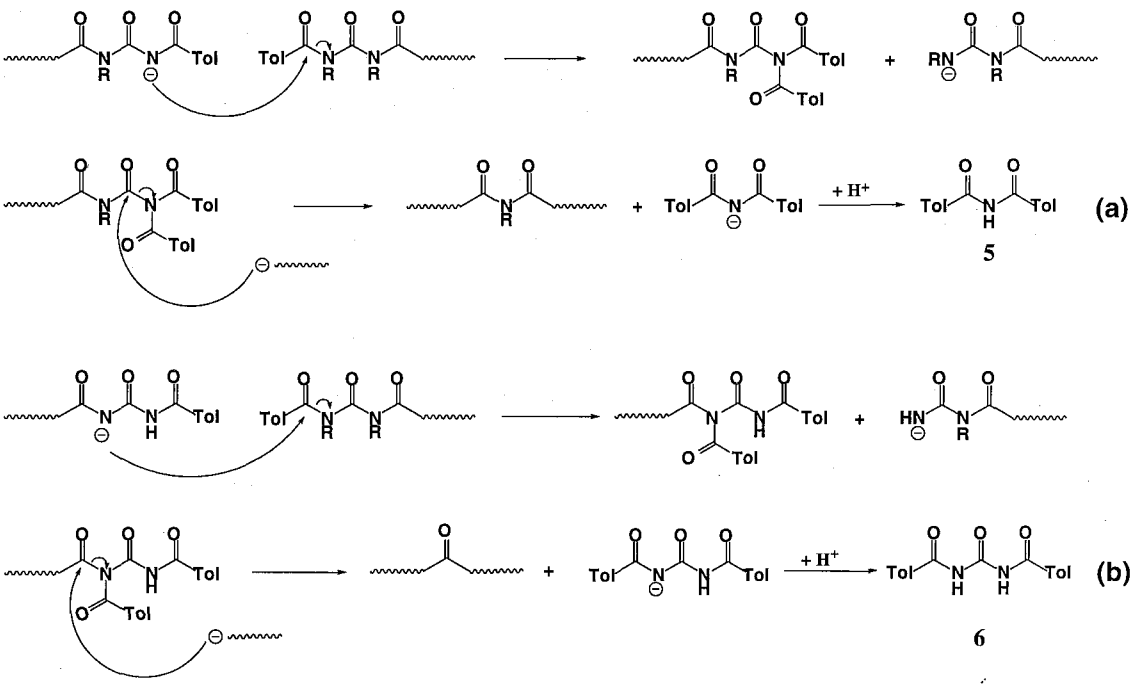


Scheme 3

In contrast to *t*-BuOK, 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) (3 mol%) as the initiator conducted not only the hydrogen-transfer but also the vinyl polymerization, which could be clearly supported by the ^{1}H NMR spectra. For instance, in the ^{1}H NMR spectrum of the polymer

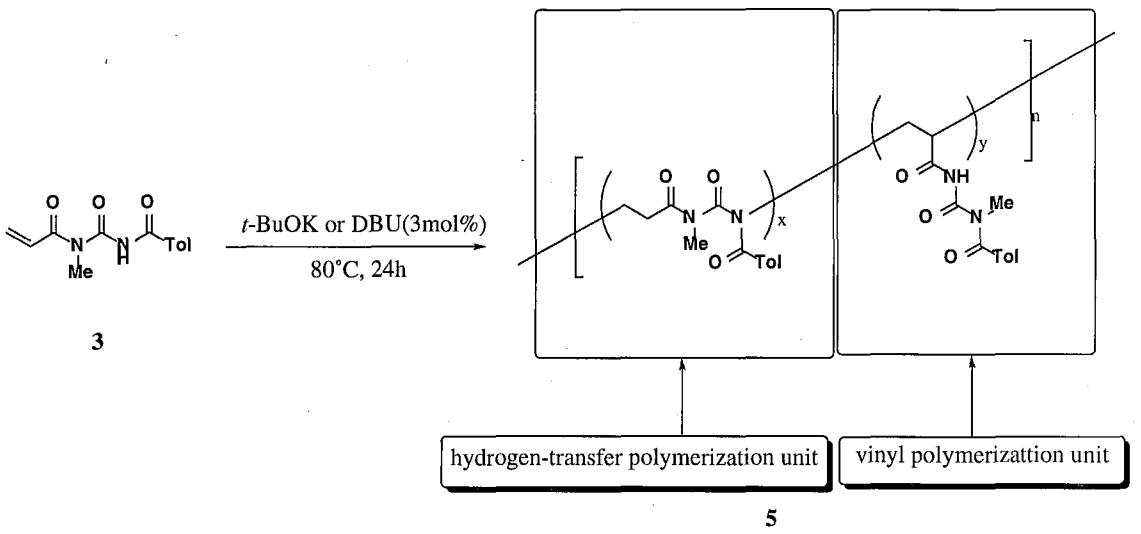
obtained in run 5 (Figure 1b), the peaks attributable to methine and methylene protons formed by the vinyl polymerization at δ 1.50 - 2.20 ppm together with the peaks due to the hydrogen-transfer polymerization unit were observed. The proportion of the vinyl polymerization was evaluated from the relative peak area (z = 16-20%) (runs 5-8 in Table 1), which seems to be independent on the solvents. The counter cation (the ammonium ion from DBU) may exist as a loose ion pair with the propagating end regardless the solvent. Consequently, the nucleophilicity of the carbanion (ii) might be strong enough to induce the vinyl polymerization.

It should be noted that, in the ^{1}H NMR spectra of polymer **3**, the peak area of the aromatic protons was smaller than expected (Table 1: runs 1-4, by 29-48%; runs 5-8, by 38-57%). Low molecular-weight compounds consisted of the eliminated aromatic parts from the monomer and/or the polymer were detected in the diethyl ether-soluble part, from which 4,4'-dimethylbenzimide (**5**) and *N,N'*-(4-methylbenzoyl)urea (**6**) were isolated in 24% and 10% yields, respectively (Table 1, run 3). One possible explanation of the path generating **5** is shown in Scheme 4a. That is, the propagating *N*-anion attacks the carbonyl group in x unit or y unit, and the resulting or another propagating *N*-anion attacks the imide carbonyl group to give an anion of **5**. In a similar way, *N,N'*-(4-methylbenzoyl)urea (**6**) might be produced starting from another *N*-anion (Scheme 4b).



Scheme 4. Possible Mechanism for Elimination Reactions

Hydrogen-transfer Polymerization of 2. In order to exclude one of the two active hydrogens in the hydrogen-transfer polymerization, monomer **2** was prepared from 4-methylbenzoyl isocyanate and *N*-methylacrylamide and subjected to the polymerization under the same conditions (Scheme 5). Similarly to the polymerization of **1**, *t*-BuOK could selectively undertake the hydrogen-transfer polymerization, while DBU partially induced the vinyl polymerization (Table 2). Figure 2 shows the ^{1}H-NMR spectrum of polymer **4** obtained in run 3 using *t*-BuOK as the initiator, supporting the exclusive hydrogen-transfer polymerization.



3

5

Scheme 5

Table 2. Hydrogen-Transfer Polymerization of *N*-Acryloyl-*N*-methyl-*N'*-4-methylbenzoylurea (**2**)[a)]

Run	Initiator	Solvent	Conv. (%)[b)]	Yield (%)[c)]	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$)[d)]	x / y [b)]
1	*t*-BuOK	DMF	95	21	4700 (1.16)	100 / 0
2	*t*-BuOK	DMSO	93	12	4500 (1.13	100 / 0
3	*t*-BuOK	MeCN	91	14	5300 (1.14)	100 / 0
4	*t*-BuOK	PhMe	94	16	4600 (1.11)	100 / 0
5	DBU	DMF	94	14	3000 (1.39)	56 / 44
6	DBU	DMSO	100	12	2800 (1.39)	61 / 39
7	DBU	MeCN	97	18	1900 (1.47)	60 / 40
8	DBU	PhMe	96	21	1600 (1.53)	67 / 33

a) Conditions: [**2**] = 1 *M*, initiator (3 mol%), inhibitor : *N*-phenyl-*β*-naphthylamine (1 mol%), 80°C, 24h.
b) The ratio of x to y in Scheme 5, determined by ^{1}H NMR spectra.
c) Diethyl ether-Insoluble part.
d) Estimated by GPC based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

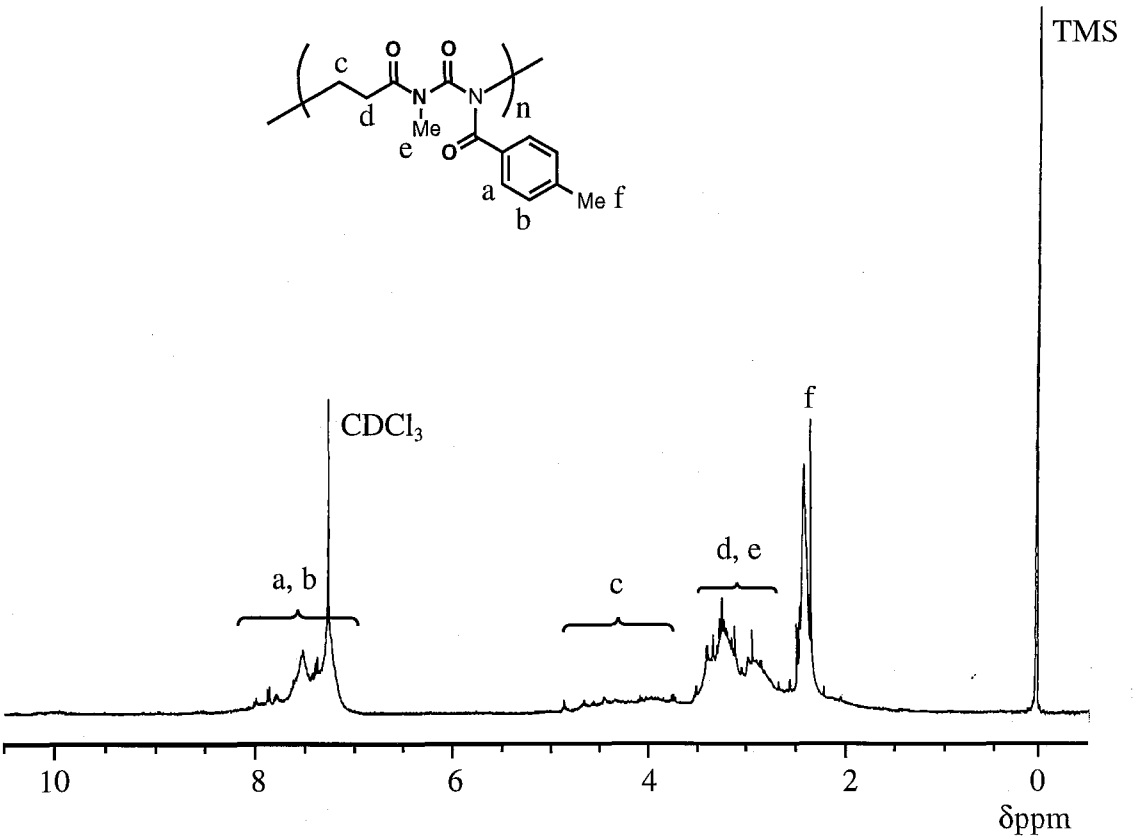
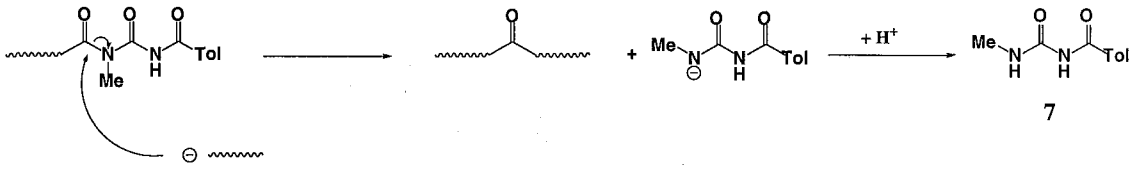


Figure 2 ^{1}H-NMR spectrum of **4** (in $CDCl_3/CF_3COOH$, v/v=4/1).

^{1}H NMR spectra of **4** produced by using DBU (3 mol%) showed peaks due to both of the hydrogen-transfer and the vinyl polymerization units, whose ratio was determined as x : y = 56 : 44 - 67 : 33 (Table 2, runs 5-8). Similar to the case of polymer **3**, the peak area of the aromatic protons observed in the ^{1}H NMR spectrum of polymer **4** was smaller than expected (Table 2: runs 1-4, by 0-4 %; runs 5-8, by 53-67%). In this case, the *N*-methyl-*N'*-4-methylbenzoylurea (**7**) was isolated in 20% yield from the diethyl ether-soluble part (run 5). This result may indicate the existence of any side reactions occurring mainly from the vinyl polymerization unit. One possible path for **7** may include the nucleophilic attack of the propagating *N*-anion toward the another vinyl polymerization unit (Scheme 6). Although the reason for the relative

increase of the hydrogen-transfer process in comparison with the case of **1** is not clear, the results of the polymerization of **2** supported further that the imide proton participates in the hydrogen-transfer process.



Scheme 6. Plausible Reaction Path for *N*-Methyl-*N'*-4-methylbenzoylurea (**7**)

5.3 Experimental

Materials. *N,N*-Dimethylformamide (DMF), dimethylsulfoxide (DMSO), acetonitrile (MeCN), and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) were dried over CaH_2, distilled, and stored under nitrogen. Toluene (PhMe) was dried over sodium metal and distilled under nitrogen atmosphere. Potassium *tert*-butoxide (*t*-BuOK) was prepared from *t*-butanol and potassium. Other commercially available reagents were used without further purification. 4-Methylbenzoyl isocyanate was prepared from 4-methylbenzamide and oxalyl chloride by a reported method.[16)]

Measurements. IR spectra were measured on a JASCO FT/IR-5300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-EX90 (^{1}H NMR: 90 MHz and ^{13}C NMR: 22.4 MHz) or JEOL JNM-EX400 (^{1}H NMR: 400 MHz and ^{13}C NMR: 100 MHz) spectrometer. Number- and weight-average molecular weights ($\overline{M}_n$ and $\overline{M}_w$, respectively) and molecular weight distributions ($\overline{M}_w/\overline{M}_n$) were estimated by gel permeation chromatography (GPC) on a Tosoh Co. HLC-8020 system equipped with polystyrene gel columns (TSK® gel G6000HXL, TSK® gel G5000HXL, TSK® gel G4000HXL, and TSK® gel G2500HXL)

using DMF containing LiBr (5.8 mM) as eluent, a flow rate of 1.0 mL/min, polystyrene calibration, and an ultraviolet (UV) detector. Fast atom bombardment mass spectra (FAB/MS) were recorded by using a JEOL JMS-700 spectrometer, whereby a mixture of a sample and *m*-nitrobenzyl alcohol on a standard FAB target was subjected to a beam of xenon atoms produced at 6 keV, 2 mA.

Synthesis of *N*-Acryloyl-*N'*-(4-methylbenzoyl)urea (1). To a 500 mL round-bottomed flask containing a THF (180 mL) solution of acrylamide (8.25 g, 0.12 mol) and *N*-phenyl-*β*-naphthylamine (0.25 g, 1.14 mmol) as a radical inhibitor was added 4-methylbenzoyl isocyanate (18.70 g, 0.12 mol) under nitrogen. After the mixture was refluxed for 2 h, the reaction mixture was evaporated to dryness under reduced pressure. The obtained white solid was recrystallized from a mixed chloroform-methanol. Yield 97% (26.13g, 0.11 mol), mp. 155-157°C.

IR (KBr): 3451(NH), 1775(C=O), 1680(C=O), 561(N-C=O)cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ: 2.44 (s, 3H, $C\underline{H}_3$-C_6H_4-), 5.97 (dd, J = 6.39 and 5.09 Hz , 1H, CH_2=C$\underline{H}$-), 6.57 (d, J = 6.39 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 6.58 (d, J = 5.09 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 7.33 (d, J = 8.46 Hz, 2H, -$C_6\underline{H}_4$-), 7.89 (d, J = 8.46 Hz, 2H, -$C_6\underline{H}_4$-), 10.54 (bs, 1H, -CON$\underline{H}$CO-), 10.83 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 21.7, 128.0, 129.2, 129.8, 131.8, 144.7, 150.6, 166.1 ppm; ANAL. Calcd for $C_{12}H_{12}N_2O_3$: C, 62.06%; H, 5.21%; N, 12.06%. Found: C, 61.87%; H, 5.11%; N, 11.95%.

Synthesis of *N*-Acryloyl-*N*-methyl-*N'*-(4-methylbenzoyl) urea (2). To a 20 mL round-bottomed flask containing a benzene (8 mL) solution of 4-methylbenzoyl isocyanate (1.92 g, 11.88 mmol) was added *N*-methylacrylamide (0.95 g, 11.13 mmol) and the mixture was stirred at room temperature for 48 h under nitrogen. The resulting mixture was evaporated to dryness and the residue was subjected to chromatography

on silica gel with chloroform as eluent to isolate **2** as white crystals, which was purified further by recrystallization from benzene. Yield 62% (1.70 g, 6.90 mmol), mp. 121-123°C.

IR (KBr): 3449 (NH), 1763 (C=O), 1666 (C=O), 766(-CH_2-), 554(N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.44 (s, 3H, $C\underline{H}_3$-C_6H_4-), 3.26 (s, 3H, $\underline{CH}_3$-N-), 5.97 (dd, *J*=7.61 and 4.32 Hz, 1H, CH_2=C$\underline{H}$-), 6.58 (d, *J*=4.32 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 6.60 (d, *J*=7.61 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 7.33 (d, *J*=8.37 Hz, 2H, -$C_6\underline{H}_4$-), 7.98 (d, *J*=8.37 Hz, 2H, -$C_6\underline{H}_4$-), 12.11 (s, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 21.6, 31.9, 127.9, 128.5, 129.6, 130.4, 132.93, 143.8, 150.3, 164.6, 170.6 ppm; ANAL. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40%; H, 5.73%; N, 11.38%. Found: C, 63.25%; H, 5.78%; N, 11.42%.

Hydrogen-Transfer Polymerization (Typical Procedure). Monomer (**1** or **2**) (1.0 *M*), *t*-BuOK or DBU (3 mol%), and *N*-phenyl-β-naphthylamine (1 mol%, an inhibitor for the radical polymerization) were dissolved in DMF, DMSO, MeCN or PhMe in a test tube under nitrogen atmosphere. After the reaction at 80°C for 24 h, the mixture was poured into diethyl ether and the precipitated polymer was dried *in vacuo.*

Polymer Obtained from 1 (Run 1 in Table 1). IR (KBr) 3444 (NH), 2934 (-CH_2-), 1690 (C=O), 1460 (-CH_2-), 1385 (C-N), 752 (-CH_2-), 553 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.47 (s, 3H×0.58, $C\underline{H}_3$-C_6H_4-), 2.60-3.55 (m, 2H, -CH_2-$C\underline{H}_2$-CO-), 3.60-4.50 (m, 2H, -N-$C\underline{H}_2$-CH_2-), 7.10-7.48 (m, 2H×0.58, CH_3-$C_6\underline{H}_4$-), 7.60-7.90 (m, 2H×0.58, CH_3-$C_6\underline{H}_4$-), 9.85 (bs, 1H×0.37, -CON$\underline{H}$CO-), 10.00 (bs, 1H×0.63, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.1, 21.4, 30.4, 30.8, 31.1, 34.2, 34.5, 35.1, 35.2, 35.3, 35.8, 36.3, 36.5, 37.6, 37.8, 38.0. 127.2, 127.5, 127.9, 128.2, 128.5, 128.7, 129.0, 129.4, 129.6, 130.0, 130.1, 131.0, 131.7, 142.9, 147.0, 147.4, 148.7, 148.9, 154.0, 166.2,

166.3, 171.1, 171.7, 172.9 ppm.

Polymer Obtained from 1 (Run 4 in Table 1). IR (KBr) 3425 (NH), 2976 (-CH_2-), 1690 (C=O), 1467 (-CH_2-), 1385 (C-N), 761(-CH_2-), 554 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 1.50-2.20 (m, 2H×0.18, -C$\underline{H}_2$-CH-), 2.44 (s, 3H×0.43, C$\underline{H}_3$-C_6H_4-), 2.55-2.72 (m, 1H×0.18, -CH_2-C$\underline{H}$-), 2.62-3.55 (m, 2H×0.82, -CH_2-C$\underline{H}_2$-CO-), 3.60-4.50 (m, 2H×0.82, -N-C$\underline{H}_2$-CH_2-), 7.10-7.48 (m, 2H×0.43, CH_3-$C_6\underline{H}_4$-), 7.60-7.90 (m, 2H×0.43, CH_3-$C_6\underline{H}_4$-), 9.85 (bs, 2H×0.38, -CON$\underline{H}$CO-), 10.00 (bs, 2H×0.62, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.1, 21.4, 30.4, 30.7, 31.1, 31.6, 34.2. 34.5, 35.1, 35.2, 35.3, 35.6, 35.7, 36.2, 37.6, 37.8, 38.0 47.9, 127.9, 128.0, 128.1, 128.5, 128.7, 129.0, 129.4, 129.6, 130.0, 130.1, 131.0,143.2, 147.1, 147.4, 148.7, 148.9, 165.4, 166.2, 166.3, 166.4, 171.7, 172.4, 173.0 ppm.

Low Molecular-Weight Products Obtained from 1 in Acetonitrile (Run 3 in Table 1). The following two compounds were isolated from the diethyl ether-soluble part of run 3 (Table 1) by column chromatography (eluent: chloroform). 4,4'-Dimethylbenzimide (**5**): Yield 24%; R_f = 0.58 (chloroform / methanol = 9/1 v/v); IR (KBr) 3400 (NH), 1718 (-CONHCO-) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.43 (s, 3H, C$\underline{H}_3$-C_6H_4-), 7.30 (d, *J*=8.40 Hz, 2H, -$C_6\underline{H}_4$-), 7.79 (d, *J*=8.40 Hz, 2H, -$C_6\underline{H}_4$-), 9.14 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 21.6, 128.0, 129.4, 130.6, 143.8, 166.6 ppm; FAB/MS *m/z* 254 $[M+H]^+$.

N,N'-(4-Methylbenzyl)urea (**6**): Yield 10%; R_f = 0.45 (chloroform / methanol = 9/1 v/v); IR (KBr) 3387 (NH), 1750 (-CONHCO-) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.45 (s, 3H, C$\underline{H}_3$-C_6H_4-), 7.35 (d, *J*=7.60 Hz, 2H, -$C_6\underline{H}_4$-) , 7.95 (d, *J*=7.60 Hz, 2H, -$C_6\underline{H}_4$-), 10.98 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 21.6, 127.9, 129.1, 129.8, 144.6, 149.8, 166.8 ppm; FAB/MS *m/z* 297 $[M+H]^+$.

Polymer Obtained from 2 (Run 3 in Table 2): IR (KBr) 3433 (NH), 2951 (-CH_2-), 1686 (C=O), 1439 (-CH_2-), 1357 (C-N), 754 (-CH_2-), 527 (N-C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.46 (s, 3H, $C\underline{H}_3$-C_6H_4-), 2.60-3.60 (m, 5H, -CH_2-$C\underline{H}_2$-CO- and -N-$C\underline{H}_3$), 3.60-4.50 (m, 2H, -N-$C\underline{H}_2$-CH_2-), 7.00-8.00 (m, 4H, CH_3-$C_6\underline{H}_4$-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 21.0, 21.2, 25.3, 28.1, 30.5, 33.0, 36.8, 127.1, 127.7, 127.6, 128.0, 128.1, 128.3, 128.5, 128.7, 128.9, 129.2, 129.5, 129.8, 130.1, 131.0, 135.4, 140.1, 142.8, 144.5, 159.0, 171.9, 173.9 ppm.

Low Molecular-Weight Product Obtained from 2 in DMF (Run 5 in Table 2). *N*-Methyl-*N'*-4-methylbenzoylurea (**7**) was isolated from the diethyl ether-soluble part of run 5 (Table 2) by column chromatography (eluent: chloroform). Yield 20%; R_f = 0.63 (chloroform / methanol = 9/1 v/v); IR (KBr) 3335 (NH), 1665 (-CONHCO-) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.42 (s, 3H, $C\underline{H}_3$-C_6H_4-), 2.96 (d, 3H, $C\underline{H}_3$-N-), 7.28 (d, *J*=8.00 Hz, 2H, -$C_6\underline{H}_4$-), 7.87 (d, *J*=8.00 Hz, 2H, -$C_6\underline{H}_4$-), 8.69 (bs, 1H, -CON$\underline{H}$CO-), 9.46 (bs, 1H, -CON$\underline{H}$CO-) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 21.6, 26.3, 127.7, 129.4, 129.6, 143.8, 155.1, 168.0 ppm; FAB/MS *m/z* 193 $[M+H]^+$.

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16) For the initiation step, two possibilities might be taken into consideration: the nucleophilic addition of the initiating anion (*t*-BuO^-) toward the unsaturated bonds of **1** and the deprotonation of the amide proton by *t*-BuO^-. In Chapter 4 (and also in ref. 9), the author has shown that the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (CH_2=CHCONHCONHTs) proceeds *via* the latter path (i.e., the elimination of N-H), which might be also plausible as the initiation step of the polymerization of **1**, as shown in Scheme 5.

Chapter 5

Chapter 6

Hydrogen-Transfer Polymerization of Vinyl Monomers Having Acylurea Moieties Derived from *p*-Tolyl Isocyanate and Acrylamide Derivatives

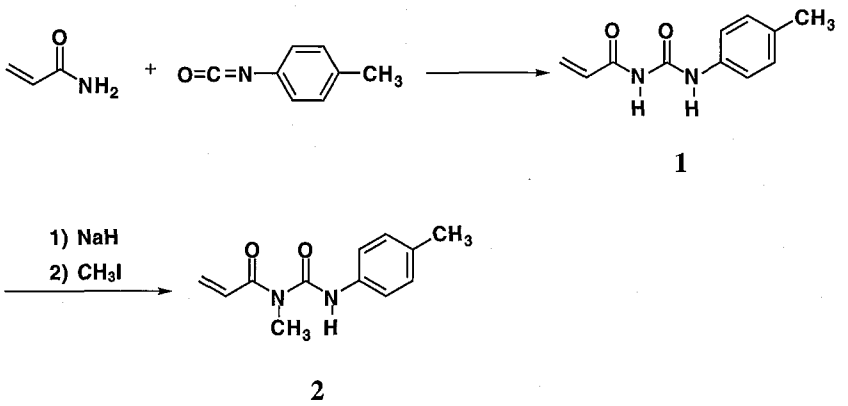
Abstract

The anionic polymerization of *N*-acryloyl-*N'*-*p*-tolylurea (**1**) was carried out at 80°C in DMF, DMSO, acetonitrile or toluene containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical inhibitor for 24 h using *t*-BuOK or DBU (3 mol%) as an initiator. It was found that **1** undertook the selective hydrogen-transfer polymerization in the case of *t*-BuOK as an initiator but both hydrogen-transfer and vinyl polymerization proceeded in the case of DBU.

6.1 Introduction

Since Matlack *et al.* first reported the hydrogen-transfer polymerization of acrylamide using anionic initiators, various unsaturated amides have been evaluated their effectiveness on the hydrogen-transfer process in the polymerization. [1-5] Unlike simple vinyl polymerization systems, the hydrogen transfer polymerization merits in production of functionalized main chains. In Chapters 4 and 5, the author has described the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea and *N*-acryloyl-*N'*-(4-methylbenzoyl)urea prepared from acrylamide and activated isocyanates (i.e., *p*-toluenesulfonyl isocyanate and 4-methylbenzoyl isocyanate, respectively).[6, 7] As they have two acidic protons on the nitrogen atoms, their anionic polymerizations involved the hydrogen-transfer process and functional groups such as -CO-N(CONHX)- and -CO-NH-CO-N(X)- (X; $-SO_2R$ and -COR for *N*-acryloyl-*N'*-*p*-toluenesulfonylurea and *N*-acryloyl-*N'*-(4-methylbenzoyl) urea, respectively) can be incorporated into the main chain of the polymers.

As *N*-acryloyl-*N'*-tolylurea (**1**) has an urea moiety with two amide protons on the nitrogen atoms. The different acidity of the N-H groups in **1** may give an interesting influence on the hydrogen-transfer polymerization behavior. The polymerization of monomer **1** will offer polymers with unique functional groups (i.e., -CO-N(CONHR)- and/or -CO-NH-CO-N(R)-) in the main chain which may be of importance for new functional polymers. In this Chapter, the author describes detailed results of the hydrogen-transfer polymerization of **1** and **2** (an *N*-methylated form of **1**).



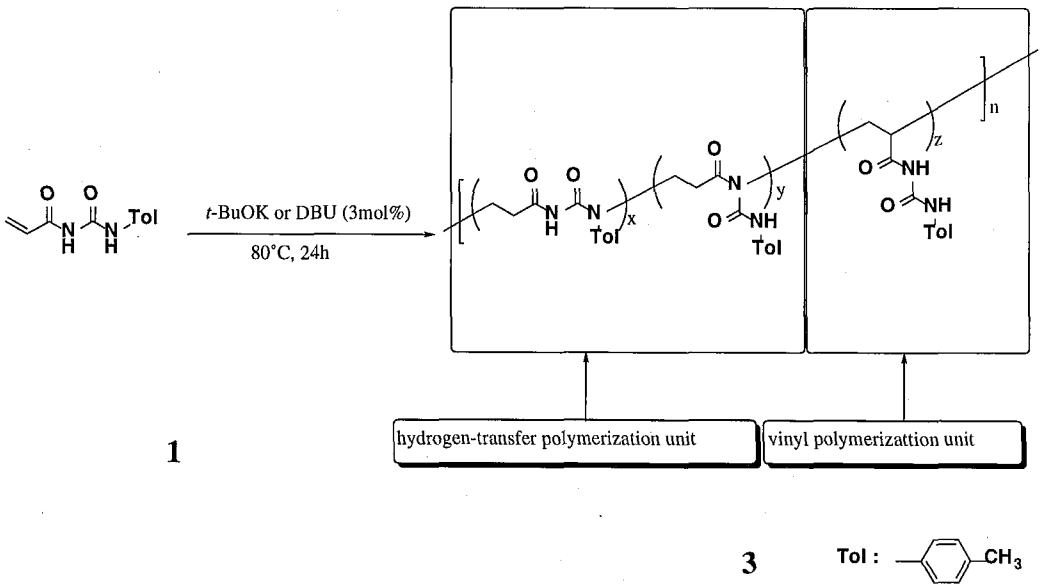
1

2

Scheme 1

6.2 Results and Discussion

Hydrogen-transfer Polymerizations of 1 and 2. The polymerization of **1** was carried out at 80°C for 24 h using *t*-BuOK (3 mol%) as an initiator in *N,N*-dimethylformamide (DMF) containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical polymerization inhibitor (Scheme 2). As a result, conversion of **1** reached to 60% and a polymer **3** ($\overline{M}_n$ = 3100) was obtained as a diethyl ether-insoluble part in 16 % yield (Table 1, run 1).



1

3

Scheme 2

Table 1 Hydrogen-Transfer Polymerization of *N*-Acryloyl-*N'*-*p*-tolylurea (**1**)[a)]

Run	Initiator	Solvent	Temp. (°C)	Time (h)	Conv. (%)[b)]	Yield (%)[c)]	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$)[d)]	x / y / z [b)]
1	*t*-BuOK	DMF	80	24	60	16	3100 (1.19)	37 / 63 / 0
2	*t*-BuOK	DMF	80	72	72	27	3200 (1.07)	36 / 64 / 0
3	*t*-BuOK	DMF	120	24	66	20	3400 (1.08)	28 / 72 / 0
4	*t*-BuOK	DMSO	80	24	58	14	2800 (1.23)	35 / 65 / 0
5	*t*-BuOK	MeCN	80	24	62	16	2800 (1.21)	33 / 67 / 0
6	*t*-BuOK	PhMe	80	24	28	2	3500 (1.24)	47 / 53 / 0
7	DBU	DMF	80	24	63	20	2900 (1.27)	30 / 43 / 27
8	DBU	DMSO	80	24	59	11	3000 (1.25)	23 / 44 / 33
9	DBU	MeCN	80	24	68	17	1900 (1.32)	37 / 42 / 21
10	DBU	PhMe	80	24	72	14	2200 (1.46)	39 / 39 / 22

a) Conditions: [**1**] = 1 *M*, initiator (3 mol%), inhibitor : *N*-phenyl-*β*-naphthylamine (1 mol%).
b) The ratio of x, y to z in Scheme 2, determined by ^{1}H NMR spectra.
c) Diethyl ether-insoluble part.
d) Estimated by GPC based on polystyrene standards, eluent: DMF containing LiBr (5.8 mM).

From the ^{1}H NMR spectrum of the obtained polymer, the hydrogen-transfer polymerization was found to proceed exclusively (Figure 1a). That is, peaks attributable to the methylenes adjacent to the nitrogen atom and those adjacent to the carbonyl group were observed at δ 3.55 - 4.50 (d, f) and 2.60 - 3.55 (e, g) ppm, respectively. The ratio of the two hydrogen-transfer units (x : y in Scheme 2) was determined by the integral ratio of the residual amide protons observed at 10.34 and 10.01 ppm. The peak area of the aromatic protons was smaller than that of the expected structure by 27%. It may be assumed that aromatic parts are eliminated from the monomer and/or the polymers, as described in Chapter 5. Actually, TLC analysis of the diethyl ether-soluble part showed several UV active spots and 1,3-di(4-methylphenyl)-1,3,5-triaza-2,4,6-trioxo-cyclooctane (**4**) was isolated in 6% (Table 1, run 5). One possible explanation of the path generating **4** is shown in Scheme 3.

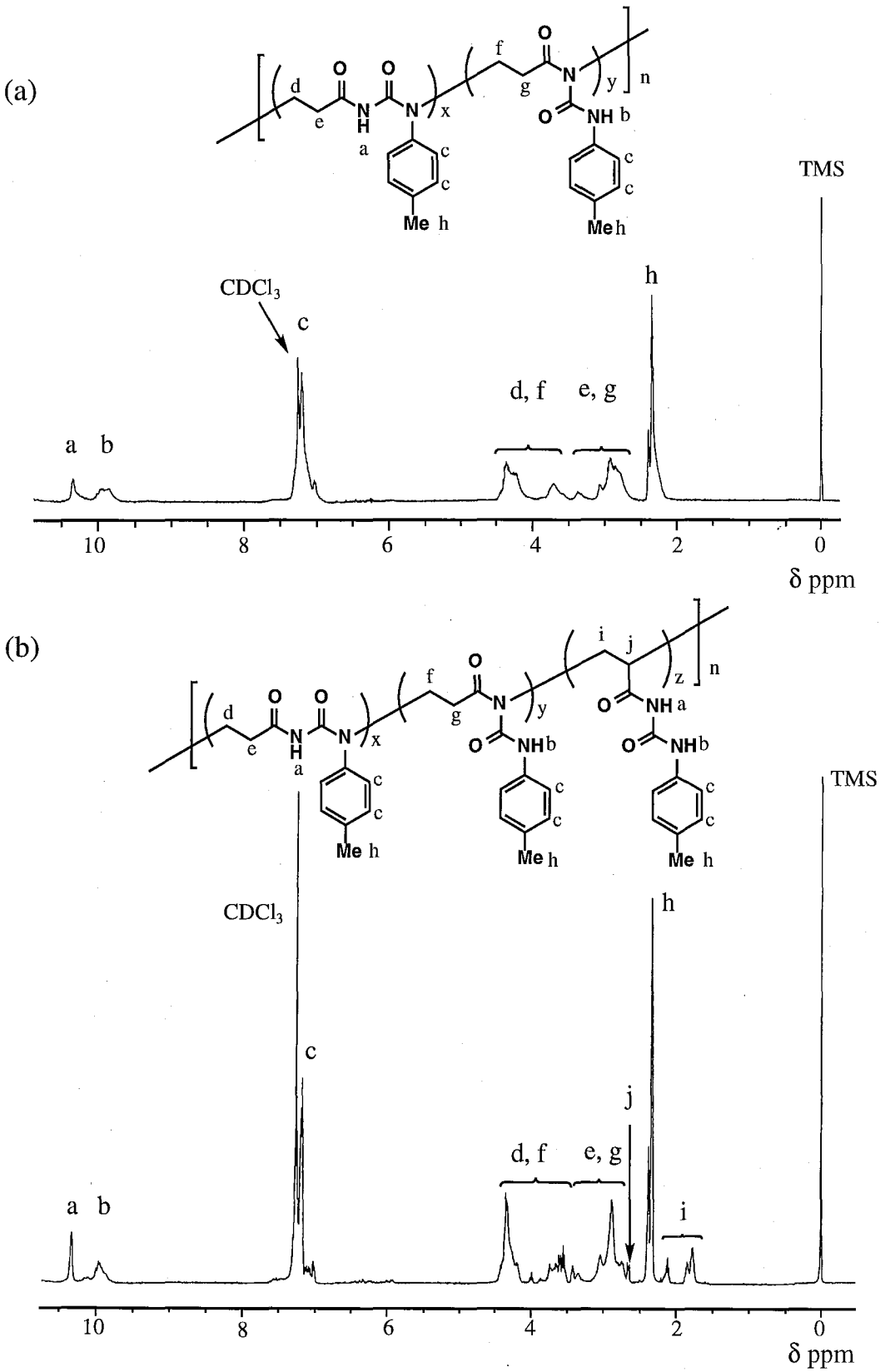
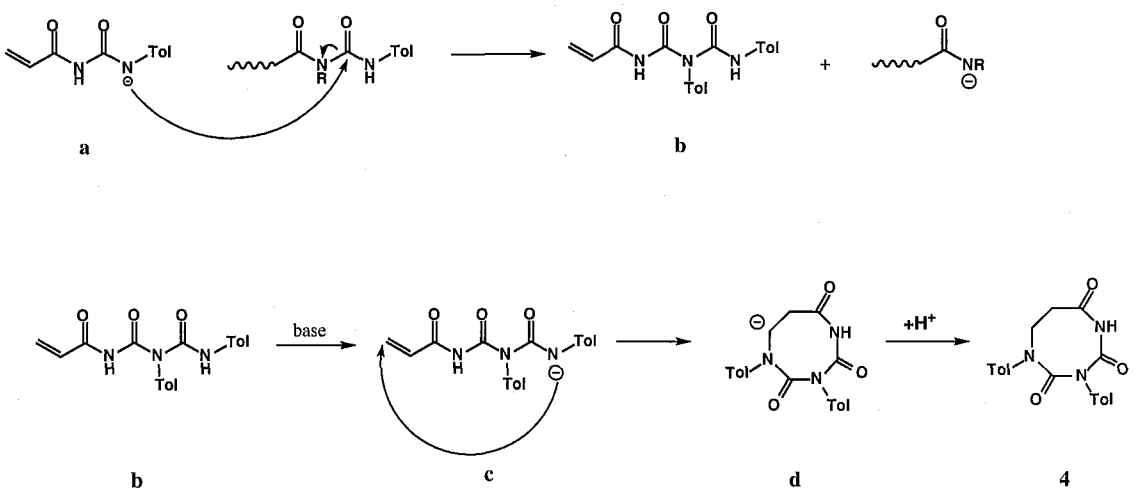


Figure 1 ^{1}H-NMR spectra (in $CDCl_3/CF_3COOH$, v/v=4/1) of **3** prepared in run 1 (a) and that prepared in run 7 (b).

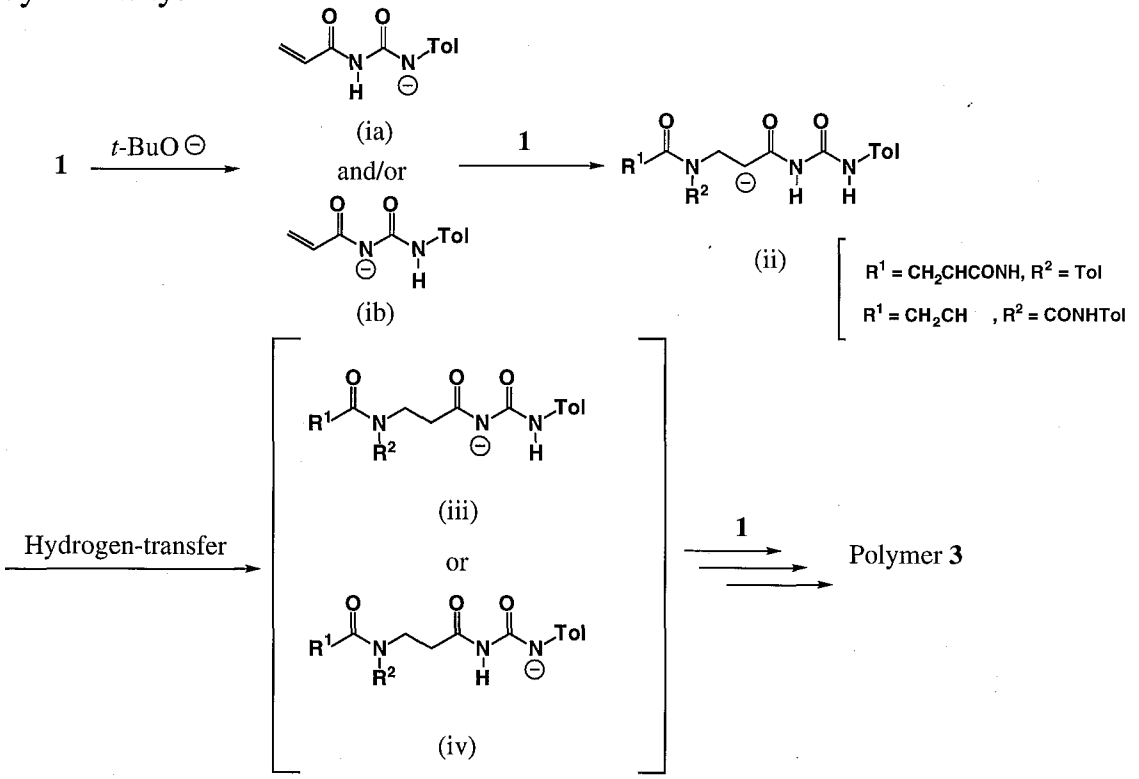


Scheme 3. Possible Mechanism for Elimination Reactions

That is, the propagating *N*-anion attacks the carbonyl group in y unit or the monomer, and the *N*-anion (**a**) generated by the deprotonation of the monomer attacks the imide carbonyl group in y unit or another monomer to give **b**. Then, the NH proton adjacent to the tolyl group of **b** is deprotonated again to generate the *N*-anion (**c**). The intramolecular cyclization of **c** leads to the production of **d** which is converted to **4** by the protonation. To increase the polymer yield, the polymerization was carried out for longer period (i.e., 72 h) (run 2). Resultantly, the conversion of **1** increased to 72% and polymer **3** was obtained in 27% yield ($\overline{M}_n$ = 3100). When the polymerization of **1** was carried out at higher temperature (i.e., 120°C), the conversion increased slightly to give **3** in a little better yield (run 3). However, the elimination of the tolyl group was much obvious than the polymer obtained in run 1 (the deficit of tolyl group: run 1, by 27% ; run 3, by 40%). These results indicated that side reactions eliminating low molecular-weight compounds from the monomer and/or the polymer may be accelerated at higher reaction temperature. Although the difference of the polymer structure was

slightly depended on the solvent (runs 1, and 4-6). The hydrogen-transfer polymerization of **1** was selectively proceeded with *t*-BuOK regardless to the solvents.

Scheme 4 shows a plausible process of the polymerization, in which an *N*-anion (ia) and/or (ib) initially generated from monomer **1** by *t*-BuOK attacks another monomer to afford an anion (ii).[9] The anion (ii) may be subsequently transformed to two kinds of *N*-anions (iii and iv) through the hydrogen-transfer process and the polymer chain may grow by this way.



Scheme 4

In contrast to the case of *t*-BuOK, polymers containing both the hydrogen-transfer and the vinyl polymerization units were obtained when 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) was used as an initiator. For instance, in the ^{1}H NMR spectrum of the polymer obtained in run 7

(Figure 1b), the peaks attributable to methine and methylene protons of the vinyl polymerization unit at δ 1.65-2.25 ppm together with those due to the hydrogen-transfer polymerization unit (δ 2.60-4.50 ppm) were observed. The proportion of the vinyl polymerization was evaluated from the relative peak area (z = 21-33%) (runs 7-10 in Table 1), which seems to be also independent of the solvents. The counter cation (the protonated form of DBU) may be less interactive to the propagating end than the case of *t*-BuOK. Consequently, the nucleophilicity of the propagating end might become stronger enough to induce the vinyl polymerization.

In order to exclude one of the two active hydrogens in the hydrogen-transfer polymerization, monomer **2** was prepared from **1** with methyl iodide and subjected to the polymerization under the same conditions. However, no polymer was produced using both *t*-BuOK and DBU. The TLC analysis of the reaction mixture revealed a lot of spots, but none of these compounds could be isolated by column chromatography or HPLC. In Chapters 4 and 5, *N*-acryloyl-*N*-methyl-*N'*-*p*-toluenesulfonylurea and *N*-acryloyl-*N*-methyl-*N'*-(4-methylbenzoyl) urea were subjected to the anionic polymerization, which did not provide polymers but low molecular-weight compounds. In these cases, reverse reactions to the monomer synthetic paths took place and the resulting isocyantes gave some adducts. [6, 7] Although we could not detect any products supporting the similar side reactions, the poor polymerizability of **2** might be due to its instability.

6.3 Experimental

Materials. *N,N'*-Dimethylformamide (DMF), dimethylsulfoxide (DMSO), acetonitrile (MeCN), and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) were dried over CaH_2, distilled, and stored under nitrogen. Toluene (PhMe) was dried over sodium metal and distilled under nitrogen atmosphere. Potassium *tert*-butoxide (*t*-BuOK) was prepared from *t*-butanol and potassium. Other commercially available reagents were used without further purification.

Measurements. IR spectra were measured on a JASCO FT/IR-5300 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-EX90 (^{1}H NMR: 90 MHz, ^{13}C NMR: 22.4 MHz) or JEOL JNM-EX400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) spectrometer. Number- (M_n) and weight-average ($\overline{M}_w$) molecular weights and molecular weight distributions ($\overline{M}_w/\overline{M}_n$) were estimated by gel permiation chromatography (GPC) on a Tosoh Co. HLC-8020 system equipped with polystyrene gel columns (TSK® gel G6000HXL, TSK® gel G5000HXL, TSK® gel G4000HXL and TSK® gel G2500HXL) using DMF containing LiBr (5.8 mM) as eluent, a flow rate of 1.0 mL/min, polystyrene calibration, and an ultraviolet (UV) detector. Fast atom bombardment mass spectra (FAB/MS) were recorded by using a JEOL JMS-700 spectrometer, whereby a mixture of a sample and *m*-nitrobenzyl alcohol on a standard FAB target was subjected to a beam of xenon atoms produced at 6 keV, 2 mA.

Synthesis of *N*-Acryloyl-*N'*-*p*-tolylurea (1). The method described for *N*-acryloyl-*N'*-phenylurea was used with slight modifications. [8] To a 500 mL round-bottomed flask containing a benzene (250 mL) solution of acrylamide (13.30 g, 0.19 mol) was added *p*-tolyl

isocyanate (25.00 g, 0.19 mol) under nitrogen. After refluxing for 44 h under nitrogen atmosphere, the mixture was cooled to room temperature to precipitate a white solid, which was recrystallized from benzene. Yield 73% (26.10 g, 0.14 mol), mp. 169-170°C.

IR (KBr): 3399(NH), 1705(C=O), 1690(C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ: 2.32 (s, 3H, $C\underline{H}_3$-C_6H_4-), 5.88 (dd, J = 9.23 and 2.60 Hz , 1H, $C\underline{H}_2$=CH- *cis*), 6.33 (dd, J = 16.79 and 9.23 Hz, 1H, CH_2=$C\underline{H}$-), 6.60 (dd, J = 16.79 and 2.60 Hz, 1H, $C\underline{H}_2$=CH- *trans*), 7.13 (d, J = 8.51 Hz, 2H, -$C_6\underline{H}_4$-), 7.42 (d, J = 8.51 Hz, 2H, -$C_6\underline{H}_4$-), 10.59 (bs, 1H, -CON$\underline{H}$-C_6H_4-), 10.77 (bs, 1H, -CON$\underline{H}$CO-) ppm. ^{13}C NMR ($CDCl_3$, 22.4 MHz), δ: 20.8, 120.4, 129.5, 129.7, 130.8, 134.0, 134.4, 152.8, 166.7 ppm; ANAL. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69%; H, 5.92%; N, 13.72%. Found: C, 64.38%; H, 5.67%; N, 13.66%.

Synthesis of *N*-Acryloyl-*N*-methyl-*N'*-*p*-tolylurea (2). To a 200 mL round bottomed flask containing a DMF (100 mL) suspension of NaH (55 wt% in oil, 2.14 g, 49.00 mmol) was added *N*-acryloyl-*N'*-*p*-tolylurea (**1**, 10.00 g, 49.00 mmol) under nitrogen. After stirring at room temperature for 24 h, methyl iodide (34.80 g, 245 mmol) was added and the mixture was stirred at ambient temperature for 7 days. The resulting mixture was extracted with diethyl ether following the addition of water. The organic phase was washed with an $Na_2S_2O_3$ aqueous solution three times, dried over $MgSO_4$, and evaporated to dryness. The residue was purified by chromatography on silica gel with hexane-chloroform (v/v 1/3) as eluent to isolate the *N'*-methylated monomer (**2**). Yield 41% (4.39 g, 20.11 mmol), mp. 78-79°C.

IR (KBr): 3436 (NH), 1705 (C=O), 1655 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ: 2.29 (s, 3H, $C\underline{H}_3$-C_6H_4-), 3.36 (s, 3H, $C\underline{H}_3$-N-), 5.86 (dd, J=9.45 and 2.79 Hz, 1H, $C\underline{H}_2$=CH- *cis*), 6.43 (dd, J=16.83 and 2.79 Hz, 1H,

$C\underline{H}_2$=CH- *trans*) , 6.72 (dd, *J*=16.83 and 9.45 Hz, 1H, CH_2=$C\underline{H}$-), 7.10 (d, *J*=8.51 Hz, 2H, -$C_6\underline{H}_4$-) , 7.41 (d, *J*=8.51 Hz, 2H, -$C_6\underline{H}_4$-), 11.44 (s, 1H, -CON$\underline{H}$-C_6H_4-) ppm. ^{13}C NMR ($CDCl_3$, 22.4 MHz), δ: 20.7, 31.7, 120.3, 128.9, 129.3, 131.1, 133.5, 135.1, 152.2, 169.6 ppm; ANAL. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04%; H, 6.47%; N, 12.84%. Found: C, 66.02%; H, 6.32%; N, 12.78%.

Hydrogen-transfer Polymerization (Typical Procedure). Monomer (**1** or **2**) (1.0 *M*), *t*-BuOK or DBU (3 mol%), and *N*-phenyl-β-naphthylamine (1 mol%, an inhibitor for radical polymerization) were dissolved in DMF, DMSO, MeCN or PhMe in a test tube under nitrogen atmosphere. After the reaction at 80°C for 24 h, the mixture was poured into diethyl ether and the isolated polymer was dried *in vacuo.*

Polymer Obtained from 1 (in Table 1, Run 1). IR (KBr) 3426 (NH), 2975 (-CH_2-), 1696 (C=O), 1466 (-CH_2-), 1385 (C-N), 763 (-CH_2-) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.25-2.45 (s, 3H×0.73, $C\underline{H}_3$-C_6H_4-), 2.60-3.55 (m, 2H, -CH_2-$C\underline{H}_2$-CO-), 3.55-4.50 (m, 2H, -N-$C\underline{H}_2$-CH_2-), 6.95-7.45 (m, 4H×0.73, CH_3-$C_6\underline{H}_4$-), 10.01 (bs, 1H×0.37, -CON$\underline{H}$-C_6H_4-), 10.34 (bs, 1H×0.63, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 20.35, 20.41, 20.66, 30.74, 31.11, 33.30, 34.20, 34.65, 35.13, 35.75, 36.41, 36.92, 37.67, 38.07,119.11, 119.31, 119.57, 128.44, 128.97, 129.29, 129.70, 131.96, 132.11, 132.53, 135.07, 136.45, 136.55, 148.61, 150.67, 150.95, 151.37, 151.70, 162.29, 168.23, 168.65, 169.91, 171.74, 172.00, 172.42, 173.30 ppm.

Polymer Obtained from 1 (in Table 1, Run 7). IR (KBr) 3428 (NH), 2975 (-CH_2-), 1699 (C=O), 1464 (-CH_2-), 1387 (C-N), 762(-CH_2-) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.65-2.25 (m, 2H×0.27, -$C\underline{H}_2$-CH-), 2.25-2.45 (m, 3H×0.51, $C\underline{H}_3$-C_6H_4-), 2.62-2.78 (m, 1H×0.27, -CH_2-$C\underline{H}$-), 2.78-3.50 (m, 2H×0.73, -CH_2-$C\underline{H}_2$-CO-), 3.50-4.50 (m, 2H×0.73, -

N-C$\underline{H}_2$-CH_2-), 6.95-7.45 (m, 4H×0.51, CH_3-$C_6\underline{H}_4$-), 9.96 (bs, 1H×0.44, -CON$\underline{H}$-C_6H_4-), 10.33 (bs, 1H×0.29, -CON$\underline{H}$CO-) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 18.87, 19.48, 20.33, 20.39, 20.66, 23.35, 25.33, 25.91, 27.60, 28.22, 30.74, 31.16, 31.56, 34.00, 34.20, 34.75, 35.07, 35.75, 36.39, 37.58, 38.11, 46.49, 47.86, 48.46, 53.33, 53.91, 119.31, 119.60, 128.42, 128.76, 128.98, 129.09, 129.29, 132.09, 132.60, 135.02, 136.45, 138.18, 148.62, 150.64, 162.29, 165.40, 168.21, 169.20, 169.93, 171.78, 173.20, 173.83, 173.99 ppm.

Low Molecular-Weight Product Obtained from 1 in Acetonitrile (in Table 1, Run 5). 1,3-Di(4-methylphenyl)-1,3,5-triaza-2,4,6-trioxo-cyclooctane (**4**) was isolated from the ether-soluble part by column chromatography (eluent: chloroform). yield 6%; IR (KBr) 3243 (NH), 3034 (-C_6H_4-), 2924, 2857(-CH_2-), 1713 (-CONHCO-), 1473 (-CH_2-) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.30 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.41 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.93 (t, J = 6.40 Hz , 2H, -CH_2-C$\underline{H}_2$-CO-), 4.26 (t, J = 6.40 Hz, 2H, -N-C$\underline{H}_2$-CH_2-), 7.08 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 7.11 (d, J = 8.00 Hz, 2H, -$C_6\underline{H}_4$-), 7.31 (d, J = 8.00 Hz, 2H, -$C_6\underline{H}_4$-), 7.34 (d, J = 8.40 Hz, 2H, -$C_6\underline{H}_4$-), 10.78 (bs, 1H, -CON$\underline{H}$CO-) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 20.8, 21.20, 31.78, 36.68, 120.32, 128.21, 129.54, 129.93, 130.18, 131.94, 134.66, 139.20, 150.46, 154.72, 169.19 ppm; FAB/MS m/z 338 $[M+H]^+$.

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9) As the initiation step, two possibilities might be taken into consideration. Those are the nucleophilic addition of *t*-BuO^- toward the unsaturated bonds of **1** and the deprotonation of the amide proton by *t*-BuO^-. In Chapter 4 (and also in ref. 6), the author could support that the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (CH_2=CHCONHCONHTs) proceeds *via* the latter path (i.e., the deprotonation from N-H), which might be also plausible as the initiation step of the polymerization of **1**, as shown in Scheme 3.

Chapter 6

Chapter 7

Summary

In this thesis, the author has described the synthesis of novel polymers based on high reactivity of activated isocyanates as a new methodology for macromolecular design.

In **Chapter 2**, the author has described the synthesis and the radical polymerization of a monomer having an *N*-acyl-*N'*-sulfonylurea moiety. The monomer, *N*-acryloyl-*N'*-*p*-toluenesulfonylurea was easily prepared from *p*-toluenesulfonyl isocyanate with acrylamide. The radical polymerization was carried out at 60°C in *N,N*-dimethylformamide, dimethylsulfoxide, or 1-methyl-2-pyrrolidone by use of 2,2'-azobisisonitronitrile (3 mol%) as an initiator to give a polymer in good yields (83-94%) ($\overline{M}_n$ = 30000-715000). Copolymerization parameters of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea (M_1) were evaluated by the copolymerization with methyl methacrylate (M_2). The monomer reactivity ratios are r_1 = 2.41 and r_2 = 0.30, from which the Alfrey-Price *Q*-*e* values are estimated as Q = 3.10 and e = 0.97. Although the reason for the rather large Q value (3.10) is not clear, the e value (0.97) reflects the electron-withdrawing character of the substituent. Poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea) was readily hydrolyzed in 1 *M* NaOH solution at room temperature to give poly(acrylic acid). This higher activity in hydrolysis of the *N*-acyl-*N'*-*p*-toluenesulfonylurea group than ordinary amide moieties is discussed in Chapter 3.

In **Chapter 3**, the author has described the reaction of *p*-toluenesulfonyl isocyanate with some polymers having amide moieties in the side chain and hydrolysis of the obtained polymers. For example, poly(acrylamide) was refluxed with an excess amount of *p*-toluenesulfonyl isocyanate in tetrahydrofuran for 50 h to obtain a structurally modified

polymer in 76% yield whose sulfonylurea functionality was 100%. The resulting polymer was subjected to hydrolysis in 1*M* NaOH aqueous solution at 50°C to convert 90% of the sulfonylurea to the carboxylic acid moieties. The reason for the higher activity in hydrolysis of *N*-acyl-*N'*-*p*-toluenesulfonylurea moieties than ordinary amides was proposed to be originated from the intramolecular-hydrogen bonding between the N-H adjacent to the sulfonyl group and the oxygen of amide-carbonyl group. Owing to the increase in δ^+ character of the amide-carbonyl group, *N*-acyl-*N'*-*p*-toluenesulfonylurea derivatives might be easily attacked by hydroxide anion chemoselectively at this position.

In **Chapter 4**, the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-toluenesulfonylurea has been described. The hydrogen-transfer polymerization was carried out at 80°C for 24 h in *N,N*-dimethylformamide, dimethylsulfoxide, acetonitrile, or toluene containing *N*-phenyl-*β*-naphthylamine (1 mol%) as a radical inhibitor using potassium *tert*-butoxide or 1,8-diazabicyclo[5,4,0]undec-7-ene (3 mol%) as an initiator. In all cases, polymers were obtained in moderate yields (9-30%). The polymer structure was dependent upon the initiator and the polymerization solvent. The polymers prepared by potassium *tert*-butoxide in polar solvents (*N,N*-dimethylformamide, dimethylsulfoxide) were selectively composed of the hydrogen-transfer polymerization unit, while those prepared in less polar solvents (acetonitrile or toluene) were composed of both the hydrogen-transfer and the vinyl polymerization units. All polymers prepared by 1,8-diazabicyclo[5,4,0]undec-7-ene also contained both of these units regardless of the polymerization solvent.

In **Chapter 5**, the author has described the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-(4-methylbenzoyl)urea, which was easily prepared from 4-methylbenzoyl isocyanate with acrylamide. The hydrogen-transfer polymerization was carried out at 80°C for 24 h in *N,N*-dimethylformamide, dimethylsulfoxide, acetonitrile or toluene by potassium *tert*-butoxide or 1,8-diazabicyclo[5,4,0]undec-7-ene (3 mol%) as an initiator to produce polymers in good yields (40-62%). The structure of the obtained polymer was dependent upon the initiator used; potassium *tert*-butoxide selectively conducted the hydrogen-transfer polymerization, while 1,8-diazabicyclo[5,4,0]undec-7-ene partially induced the vinyl polymerization (16-20%).

In **Chapter 6**, the author has described the hydrogen-transfer polymerization of *N*-acryloyl-*N'*-*p*-tolylurea, which was prepared by refluxing tolyl isocyanate with acrylamide in benzene. The hydrogen-transfer polymerization was carried out at 80°C for 24 h in *N,N*-dimethylformamide, dimethylsulfoxide, acetonitrile or toluene containing *N*-phenyl-β-naphtylamine (1 mol%) as a radical inhibitor using potassium *tert*-butoxide or 1,8-diazabicyclo[5,4,0]undec-7-ene (3 mol%) as an initiator. In all cases, polymers were obtained in moderate yields (2-27%). The polymer structure was also dependent upon the initiator used; the hydrogen-transfer polymerization selectively took place in the case of potassium *tert*-butoxide as an initiator, while both of the hydrogen-transfer and the vinyl polymerization proceeded in the case of 1,8-diazabicyclo[5,4,0]undec-7-ene.

As summarized above, activated isocyanates are useful for facile structural modifications of monomers and polymers bearing weak

nucleophilic moieties such as amides. These polymers having NH and carbonyl groups may be used for molecular recognition and chelate polymers. From point of view of a polymer drug, the polymers having *N*-acyl-*N'*-sulfonylurea moieties (especially, the polymers obtained in Chapters 2 and 3) are expected to release bioactive compounds such as sulfonylurea derivatives. The fact that poly(methacrylamide) derivatives can be modified by *p*-toluenesulfonyl isocyanate and that the resulting polymers undertake hydrolysis under mild conditions might be of importance for stereoregularity analysis of poly(methacrylamide)s. The modified monomers from acrylamide derivatives give rise to novel polymers containing β-peptide structures *via* the hydrogen-transfer polymerization. Since β-alanine acts as a transmitter in the central nervous system, and β-peptide such as anserine and carnosine are known to have an inhibitory effect on cardiac movement, the polymers having β-peptide structures may perform an important part in the fields of medical science and pharmacy.

The author hopes the study described in this thesis will make any contributions to the development of polymer chemistry and other scientific fields in the future.

Chapter 7

List of Presentations

1) Synthesis and Radical Polymerization of *N*-Acryloyl-*N'*-*p*-Toluenesulfonylurea.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 70 th Annual Meeting of Chem. Soc. Jpn., Book of Abstr. II,* 777 (Tokyo, Mar. 1996).

2) Synthesis and Reaction of Poly(*N*-acryloyl-*N'*-*p*-toluenesulfonylurea).
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 45 th Annual Meeting of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **45**, 138 (Nagoya, May 1996).

3) Anionic Polymerization Behavior of Acrylamide Derivative Obtained from Acrylamide and *p*-Toluenesulfonyl Isocyanate.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 45 th Annual Meeting of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **45**, 188 (Nagoya, May 1996).

4) Anionic Polymerization Behavior of Acrylamide Derivatives Obtained from Acrylamide with *p*-Toluenesulfonyl Isocyanate.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 45 th Polymer Symposium of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **45**, 1335 (Hiroshima, Oct. 1996).

5) Anionic Polymerization Behavior of Acrylamide Derivatives Obtained from Acrylamide with 4-Methylbenzoyl Isocyanate.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 72 th Annual Meeting of Chem. Soc. Jpn., Book of Abstr. II,* 727 (Tokyo, Mar. 1997).

6) Anionic Polymerization Behavior of Monomers Synthesized from *p*-Toluenesulfonyl Isocyanate and Viniyl Compounds Having Active Hydrogens.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 46 th Annual Meeting of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **46**, 172 (Tokyo, May 1997).

7) Polymer Reaction of Poly(acrylamide) Derivatives with *p*-Toluenesulfonyl Isocyanate and Their Hydrolytic Behavior.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 46 th Annual Meeting of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **46**, 304 (Tokyo, May 1997).

8) Anionic Polymerization Behavior of a Monomer Derived from Acrylamide with Activated Isocyanate.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 46 th Polymer Symposium of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **46**, 1163 (Nagoya, Oct. 1997).

9) Reaction of *p*-Toluenesulfonyl Isocyanate with Poly(acrylamide) Drivatives and Hydrolysis Behavior of the Obtained Polymer.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 46 th Polymer Symposium of the Society of Polymer Science, Japan, Polym. Prepr. Jpn.*, **46**, 1629 (Nagoya, Oct. 1997).

10) Anionic Polymerization Behavior of *N*-Acylacrylamide Derivatives.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *The 73 th Annual Meeting of Chem. Soc. Jpn., Book of Abstr. II,* 000 (Kyoto, Mar. 1998).

List of Publications

Chapter 2 Synthesis and Radical Polymerization of Vinyl Monomer Having Sulfonylacylurea Moiety and Hydrolysis of the Obtained Polymer.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *J. Polym. Sci. Part A: Polym. Chem. in press.*

Chapter 3 Reaction of *p*-Toluenesulfonyl Isocyanate and Polymers Having Amide Moieties and Hydrolysis of the Obtained Polymer.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *Bull. Chem. Soc. Jpn. in preparation.*

Chapter 4 Novel Hydrogen-Transfer Polymerization of Vinyl Monomer Derived from *p*-Toluenesulfonyl Isocyanate and Acrylamide.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *J. Polym. Sci. Part A: Polym. Chem. in press.*

Hydrogen-Transfer Polymerization of Vinyl Monomers Derived from *p*-Toluenesulfonyl Isocyanate and Acrylamide Derivatives.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *Bull. Chem. Soc. Jpn. submitted.*

Chapter 5 Hydrogen-Transfer Polymerization of Vinyl Monomers Derived from 4-Methylbenzoyl Isocyanate and Acrylamide Derivatives.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *J. Polym. Sci. Part A: Polym. Chem. submitted.*

Chapter 6 Hydrogen-Transfer Polymerization of Vinyl Monomers Derived from *p*-Tolyl Isocyanate and Acrylamide Derivatives.
Takeru Iwamura, Ikuyoshi Tomita, Masato Suzuki, and Takeshi Endo, *Reactive & Functional Polymers. in press.*

Other Publication

Total Synthesis of (2*S*,3*S*,4*R*)-2-[(2'*R*)-2-Benzoyloxydocosanoylamino]-16-methylheptadecane-1,3,4-triol 3,4-Dibenzoate, a Partially Protected Ceramide Part of Sponge Cerebrosides.
Hideki Nakashima, Norihiko Hirata, Takeru Iwamura, Yoshiro Yamagiwa, and Tadao Kamikawa, *J. Chem. Soc. PERKIN TRANS. I,* 2849 (1994).

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