Synthesis and Polymerization of Styrene Monomer Carrying Isothiocyanate Moiety and Its Copolymerization with HEMA Based on Chemo-selectivity to Nucleophiles

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ABSTRACT: Isothiocyanate is a very useful functional group for post-polymerization modification by the reaction with amine or alcohol. An isothiocyanate monomer, 4-vinylbenzyl isothiocyanate, was synthesized from 4-vinylbenzyl chloride without using any harmful reagents such as thiophosgene and CS_2. The obtained monomer was successively polymerized by the conventional radical polymerization (AIBN, 1,4-dioxane, 60 °C) to afford the corresponding polymer. The obtained polymer was characterized by ^1H NMR, FTIR, thermogravimetric analysis (TGA), and differential scanning calorimetry. In contrast to the isocyanate group, the isothiocyanate group was relatively tolerant to alcohols, and this character enabled us to synthesize a copolymer of 4-vinyl benzylisothiocyanate and (2-hydroxyethyl methacrylate). The copolymer is transformed into networked polymer by 1,8-diazabicyclo[5.4.0]undec-7-ene as a promoter of the reaction between isothiocyanate and alcohol to afford thiocarbamate. The formation of networked polymer was characterized by FTIR and TGA. © 2013 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2013**, *51*, 5215–5220

KEYWORDS: copolymerization; isothiocyanate; modification; polystyrene; radical polymerization

INTRODUCTION Isothiocyanate (−N=C=S) group have analogies with isocyanate (−N=C=O); these groups react with amine to give corresponding thiourea and urea, respectively,[1,2] and this reaction has been used for a reliable way to link two different compartments.[3] However, reactivities against alcohol are completely different between isothiocyanate and isocyanate. Thus, isocyanates react with alcohol to afford carbamates, although isothiocyanates usually react with alcohol to give thiocarbamates very slowly.[4] The tardy reaction of isothiocyantate against alcohol or water is advantageous to apply to bioconjucation,[5–7] which require the chemo-selectivity toward amine over water and alcohol.

There are some report for the polymer bearing isothiocyanate,[8] and the synthesis and polymerization of 4-(isothiocyanate) styrene was reported in litaratures.[9–11] This monomer can be synthesized from 4-amino styrene by the use of CS_2 or thiophosgene which is not desirable from the environmental standpoint.[9,10] As a more easily accessible styrene-based isothiocyanate monomer, we focused on the 4-vinylbenzyl chloride. This monomer can be prepared from 4-chloromethyl styrene in a single step,[12] and the process does not require the use of any harmful reagents such as CS_2 and thiophosgene. To the best of our knowledge, there are no reports concerning direct polymerization of 4-vinylbenzyl isothiocyanate monomer itself to date in contrast to existing many examples concerning the UV-triggered rearrangement of thiocyanate polymer to isothiocyanate polymer.[13–17]

In this study, we present the utility of 4-vinylbenzyl isothiocyanate as the monomer for a synthesis of polymer bearing isothiocyanate group. In addition, we demonstrate that the characteristic reactivity toward alcohol would be also useful for the copolymerization with 2-hydroxyethyl methacrylate (HEMA) which has an alcohol group. The reaction between isothiocyanate and alcohol to form gel was promoted by the addition of base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

EXPERIMENTAL

Materials

4-Vinylbenzyl chloride (**1**) was obtained from AGC Seimi Chemicals (Kanagawa, Japan). KSCN, NaI, DBU, tetrahydrofuran (THF), and *N*,*N*-dimethylformadmie (DMF) were purchased from Wako Pure Chemical Industries and used as received. Azobisisobutyronitrile (AIBN) (Wako Pure Chemical Industries) was recrystallized from methanol before use. 1,4-Dioxane (Wako Pure Chemical Industries) was distilled from $LiAlH_4$ and used immediately.

Measurements

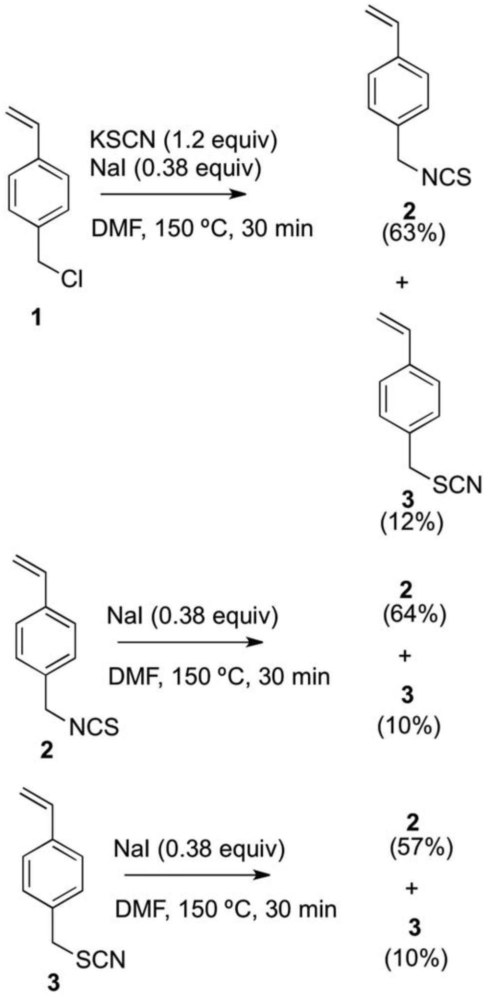
^{1}H and ^{13}C NMR spectra were recorded on JEOL-ECS400. IR spectra were recorded on a Thermo Scientific Nicolet iS10 spectrometer. Number average molecular weight (M_n) and polydispersity index (M_w/M_n) were estimated by size exclusion chromatography (SEC) using THF as an eluent at a flow rate of 0.6 mL/min at 40 °C, performed on Tosoh chromatograph model HLC-8320 system equipped with Tosoh TSKgel SuperHM-H styrogel columns (6.0 mm $\phi \times$ 15 cm, 3- and 5-μm bead sizes), refractive index detector, and UV–visible detector (254 nm). The molecular weight calibration curve was obtained with polystyrene standards. Differential scanning calorimetry (DSC) was carried out with DSC-6200 (Seiko Instrument Inc.) using an aluminum pan under 20 mL/min N_2 flow at the heating rate of 5 °C/min. Thermal gravimetric analysis (TGA) was performed with TG-DTA 6200 (Seiko Instruments Inc.) using an alumina pan under a 50 mL/min N_2 flow at the heating rate of 10 °C/min.

Synthesis of 4-Vinylbenzyl Isothiocyanate (2)

This compound was synthesized according to the reported method.[12] 4-Vinylbenzyl chloride (**1**) (7.60 g, 50 mmol) was dissolved with DMF (30 mL), and KSCN (5.82 g, 60 mmol), and NaI (2.80 g, 18.7 mmol) was added. The mixture was heated to 150 °C and stirred for 30 min. After cooled to room temperature, the solution was diluted with Et_2O (150 mL), and washed with saturated NH_4Cl aq. (100 mL). The water layer was extracted with Et_2O (150 mL × 3), the combined organic layer was washed with saturated NH_4Cl aq. (100 mL), and dried over anhydrous Na_2SO_4. After filtration, the solution was evaporated and purified by silica gel column chromatography (eluent; AcOEt:*n*-hex = 1:30) to afford pale yellow oil (4.90 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.42 (d, 2H, *J* = 8.1 Hz; ArH), 7.27 (d, *J* = 8.1 Hz, 2H; ArH), 6.71 (dd, *J* = 17.6, 10.9 Hz, 1H; Ph—C*H*═CH_3), 5.77 (d, *J* = 17.4 Hz, 1H; Ph—CH═CH_2), 5.29 (d, *J* = 11.0 Hz, 1H; Ph—CH═CH_2), 4.69 (s, 2H; Ph—CH_2—N); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 137.7 (C1), 136.0 (Ar—*C*H═CH_2), 133.6 (ArC), 129.2 (N*C*S), 127.0 (ArC), 126.7 (ArC), 114.7 (Ph—CH═*C*H_2), 48.4 (Ph—CH_2—NCS); IR (neat): ν = 2173 (s, —NCS), 2092 (vs, —NCS), 1511 (w), 1437 (w), 1342 (w), 990 (w), 913 (w), 824 (w), 721 (w), 690 cm^{-1} (w); HRMS (*m*/*z*): calcd for $C_{10}H_9OS$, 175.0456; found, 175.0453 $[M + H]^+$.

Polymerization of 4-Vinylbenzyl Isothiocyanate (4)

To **1** (500 mg, 2.85 mmol) placed in a glass ampule tube with stirring bar was added AIBN (9.36 mg, 57 μmol) in freshly distilled 1,4-dioxane (1.4 mL). The tube was cooled, evacuated, sealed off, and heated at 60 °C for the designated period with stirring. Then the mixture was cooled to room temperature, and added to methanol (100 mL) dropwise. The resulting precipitate was collected by centrifugation (3000 rpm × 30 min), washed with methanol, and dried in reduced pressure to afford colorless solid as polymer **4**. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 6.97 (2H, ArH), 6.49 (2H, ArH), 4.67 (2H, Ph—CH_2—N), 3.4–4.0 (COOCH_2— and —CH_2CH_2OH); IR (KBr): ν = 2924 (w), 2171 (m, —NCS), 2087 (vs, —NCS), 1511 (w), 1421 (w), 1338 (w), 815 (w), 682 cm^{-1} (w).



SCHEME 1 Synthesis of 4-vinyl benzylisothiocyanate (**2**).

Model Reaction of Benzyl Isothiocyanate and 1-Propanol

Benzylisothiocyanate **5** (200 mg, 1.34 mmol) was dissolved in THF (6.7 mL) and 1-propanol (100 µL, 1. 34 mmol) (and DBU for the catalytic reaction) was added. Stirred for 6 h at 25 °C, the mixture was evaporated and purified by silica gel column chromatography. The compound characterization data of thiocarbamate **6** was identical to the one previously reported.[18]

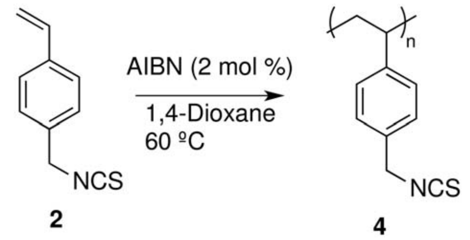
Copolymerization of 4-Vinylbenzyl Isothiocyanate (2) and HEMA

Copolymer of **2** and HEMA was prepared based on the method for homopolymer **4**. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 6.2–7.2 (ArH), 4.64 (br, Ph—CH_2—N), 4.67 (2H, Ph—CH_2—N), 0.4–2.0 (—CH_2— (main chain) and —CH_2(CH_3) —CH_2—); IR (KBr): ν = 3483 (w), 2925 (w), 2172 (s, —NCS), 2083 (s, —NCS), 1720 (m, C═O), 1512 (w), 1439 (w), 1422 (w), 1338 (w), 1185 (m), 1076 (w), 815 (w), 682 cm^{-1} (w).

Formation of Networked Polymer (8)

Copolymer **7** (30 mg, Table 3, Entry 1) was placed in a vial, and dissolved with THF (1 mL) and DBU (45 µL, 0.3 mmol)

TABLE 1 Results of Radical Polymerization of **2**



Entry	Reaction TIME (h)	Conversion[a] (%)	Yield (%)	M_n[b]	M_w/M_n[b]
1	1	19	13	12,000	1.91
2	3	24	17	12,200	1.95
3	6	39	41	14,400	2.02
4	12	62	61	13,600	2.25
5	24	82	77	15,300	2.73

[a] Estimated from ^{1}H NMR.

[b] Estimated by GPC (eluent = THF, polystyrene standards).

was added via syringe. Stirred for 6 h at room temperature, the formed pale yellow gel was collected by suction and thoroughly washed with THF and dried in vacuum to afford as pale yellow powder (33 mg). IR (KBr): ν = 2927, 2166 (s, —NCS), 2054 (s, —NCS), 1723 (m, C═O), 1644 (s, thiocarbamate), 1511, 1385, 1443, 1322, 1200, 1106, 1019, 976, 842, 813.

RESULTS AND DISCUSSION

Synthesis of 4-Vinyl Benzylisothiocyanate

The synthesis of 4-vinyl benzylisothiocyanate has been reported in the patent.[12] The reaction of 4-chloromethyl styrene (**1**) with NH_4SCN at room temperature gives thiocyanate (**3**);[16] however, the reaction with KSCN at high temperature (150 °C) afforded isothiocyanate (**2**) as a main product (Scheme 1). The IR spectrum of compound **2** showed a characteristic peak of isothiocyanate around 2100 cm^{-1},[19] and totally different from that of **3**.[16] This compound was stable and can be stored in refrigerator without any sign of decomposition at least for a week. It is noteworthy that this isothiocyanate monomer (**2**) is easy to prepare and handle and the use of harmful reagents such as thiophosgene and CS_2 was not necessary. The isomerization of thiocyanate to isothiocyanate is controlled under thermodynamic equilibrium; the reaction of **2** or **3** in the presence of catalytic amount of NaI at 150 °C gave almost a similar ratio (**2**/**3**) of the product.[20]

Homopolymerization of 4-Vinyl Benzylisothiocyanate

To the best of our knowledge, the homopolymerization of **2** has not been reported to date, although an isomerization of thiocyanate polymer into isothiocyanate by UV-irradiation has been widely used.[13–17] The polymerization reaction of **2** was performed in the presence of AIBN (2 mol %) in 1,4-dioxane at 60 °C. The reaction was quenched by adding the solution into methanol dropwise, which is not possible for the case of polymer containing isocyanate group, and the insoluble part was collected after centrifuge as the polymer **4**.

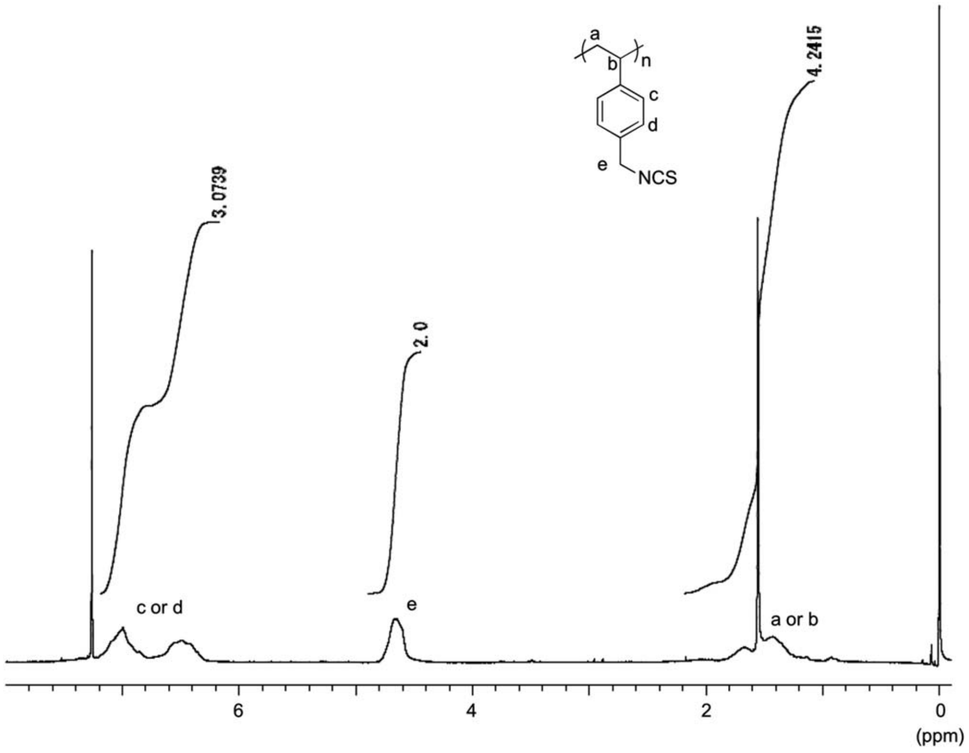


FIGURE 1 ^{1}H NMR (400 MHz) of polymer **4** in $CDCl_3$.

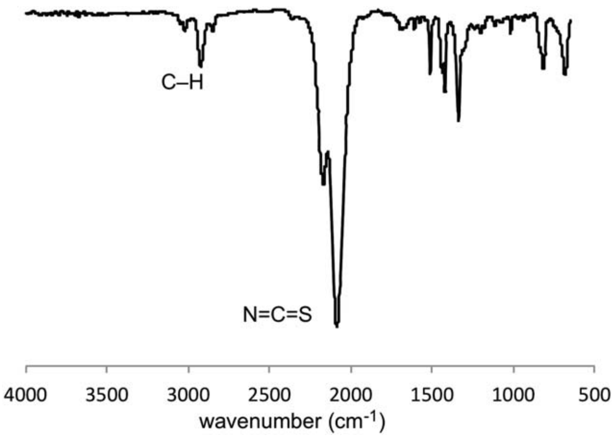


FIGURE 2 FTIR spectra of polymer **4**.

To find the ideal condition for the polymerization, we conducted the reaction with various reaction time (1 h, 3 h, 6 h, 12 h, and 24 h), and the data of each polymers were collected as shown in Table 1. The longer the reaction time was, the better the conversion of **1** and yield of polymer was. As typical for the chain polymerization, the number averaged molecular weight of polymer (M_n) was almost unchanged among those polymers, however, the M_w/M_n was increased by extending reaction time. This implies that some intramolecular reactions might proceed by the period of the reaction.

The polymer **4**, which was reacted for 6 h, was soluble (2 mg/mL) in the most of organic solvent such as DMF, DMSO, $CHCl_3$, THF, AcOEt, toluene, and acetone, but insoluble in *n*-hexane and methanol. The structure of the polymer was characterized by ^{1}H NMR and IR spectrum (Figs. 1 and 2). These spectra showed that the isothiocyanate group of the polymer was kept intact even after the free radical polymerization and the treatment with methanol.

The thermal properties of polymer **4** reacted for 6 h (Table 1, Entry 3) was also investigated by TGA and DSC analysis. The results of TG and DSC analyses of polymer **4**, reacted for 6 h (Table 1, Entry 3), are shown in Figures 3 and 4, respectively. The polymer exhibited T_{d5} (5 wt % decomposition temperature) at 314 °C and T_g (glass transition temperature) at 84 °C, being comparable to the other styrene-based polymers.

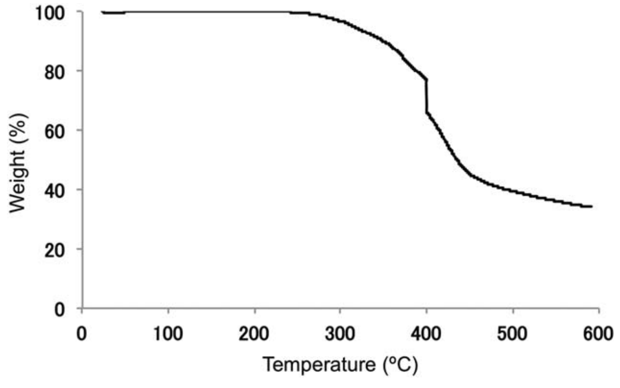


FIGURE 3 Thermogravimetric analysis of polymer **4**.

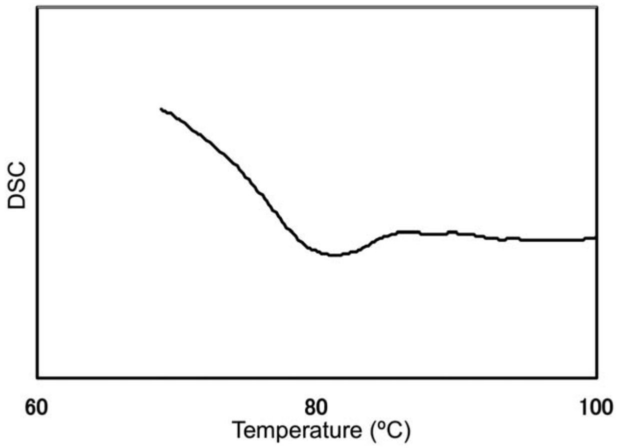


FIGURE 4 DSC analysis of polymer **4**.

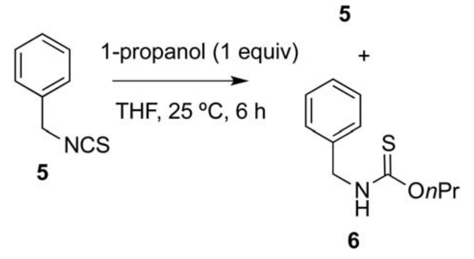
Model Reaction of Benzyl Isothiocyanate and Alcohol

To make sure the reactivity of benzyl isothiocyanate toward alcohol, model reaction was performed. The reactions of benzyl isothiocyanate and alcohol (methanol, ethanol, 1-propanol) were reported in a harsh condition;[18] however we investigated the reactivity under mild condition using benzyl isothiocyanate and 1-propanol (Table 2). To investigate the stability of isothiocyanate in alcohol, benzyl isothiocyanate was reacted with 1 equiv of 1-propanol in THF at 25 °C for 6 h. No reaction was observed by ^{1}H NMR and the benzyl isothiocyanate was recovered in 97%. To promote the reaction, we added DBU as a catalyst.[21] Although the effect of DBU was impressive, the reaction was proceeded to afford thiocarbamate (**6**) in 53% isolated yield when 0.5 equiv of DBU was used. Even with the case that 1 equiv of DBU was used, the yield of **6** was marginally improved to 69%.

Synthesis of Copolymers of 2 and HEMA

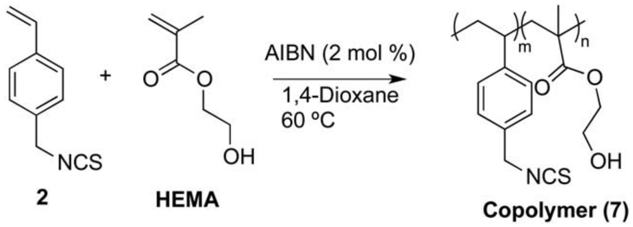
The characteristic reactivity of isothiocyanate monomer was applied to synthesize copolymers with HEMA. Three

TABLE 2 Model Reaction of Benzyl Isothiocyanate **5** and 1-Propanol



Entry	DBU (equiv)	Recovery of **5** (%)	Yield of **6** (%)
1	0	97	0
2	0.5	24	53
3	1	19	69

TABLE 3 Results of Copolymerization of **2** and **HEMA**



Entry	Feed Ratio **2**	**HEMA** (mol %)	Composition[a] **2**	**HEMA** (mol %)	Yield (%)	M_n[b]	M_w/M_n[b]
1	75	25	68	32	28	21,100	1.97
2	50	50	45	55	28	30,800	2.83
3	25	75	27	73	14	49,900	3.89

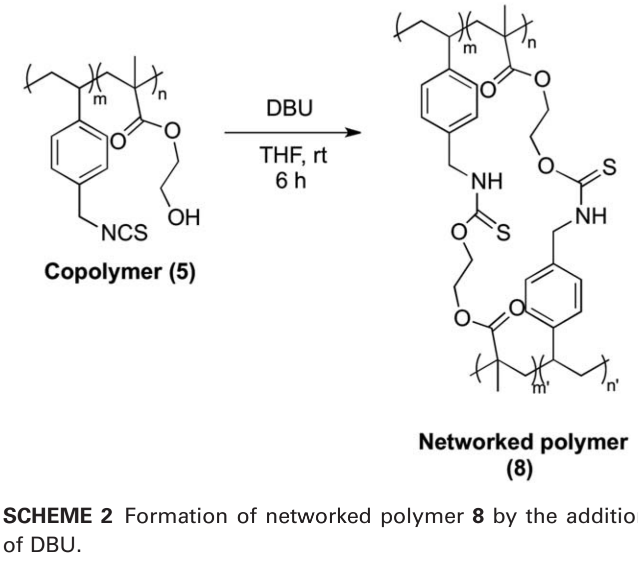
[a] Estimated from ^{1}H NMR.

[b] Estimated by GPC (eluent = THF, polystyrene standards).

copolymers, with a different ratio of **2** and HEMA as shown in Table 3, were synthesized by radical polymerization (Table 3). Polymers were obtained successively as a precipitate in MeOH. All obtained copolymer of **2** and HEMA has larger M_n than that of homopolymer of **2** by introducing HEMA unit, though M_w/M_n of copolymers also increased along with the increase of the content of HEMA; this could be partially attributed to progress of the reaction between alcohol and isothiocyanate. In addition, the reaction might have to do with the phenomenon that copolymers which contained HEMA part over 50 mol % (entry 2 and 3) became gel by standing at room temperature for several hours. Because the polymer with high HEMA content have a high local concentration of alcohol moiety enough to react with isothiocyanate even in the absence of DBU.[18]

The copolymer (**7**) composed of 68% of **2** (Table 3, Entry 1) can be transformed to the networked polymer (**8**) by the reaction of isothiocyanate and alcohol groups mediated by DBU (Scheme 2). It took 6 h to be observed as gel at room temperature and this reactivity is advantageous for application as a latent hardener. To investigate the detail of the structure of the obtained networked polymer (**8**), we performed FTIR analysis (Fig. 5) and TG analysis (Fig. 6).

The FTIR analysis of the above obtained networked polymer showed an appearance of peak around 1600 cm^{-1} which is typical of thiocarbamate. The isothiocyanate peak was remained in the IR spectrum of the networked polymer since there were remaining isothiocyanates even if the all alcohol had reacted with isothiocyanate (Fig. 5). The TG analysis of the polymer before and after the reaction exhibited an observable change. The copolymer before the reaction (**7**, Table 2, Entry 1) began its weight loss around 280 °C, and a steep weight loss was observed around 400 °C, as observed in homopolymer (**4**) (Fig. 3). In contrast, the networked polymer (**8**) began its gradual weight loss as early as around 100 °C to the point that a steep weight loss, similar to that of **4** and **5**, around 400 °C (Fig. 6). The heat-lability of networked polymer could be attributed to the thiocarbamate group formed by the reaction of isothiocyanate and alcohol.



SCHEME 2 Formation of networked polymer **8** by the addition of DBU.

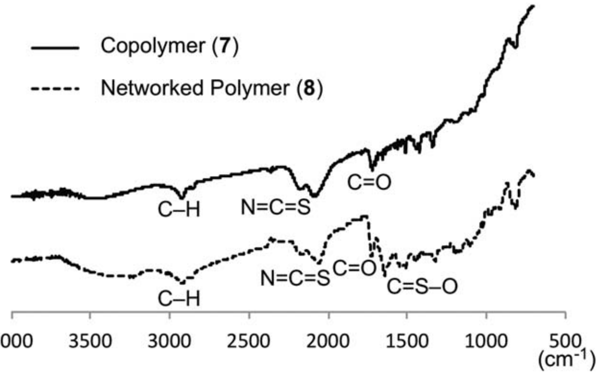


FIGURE 5 FTIR spectrum of copolymer (**7**) and networked polymer (**8**).

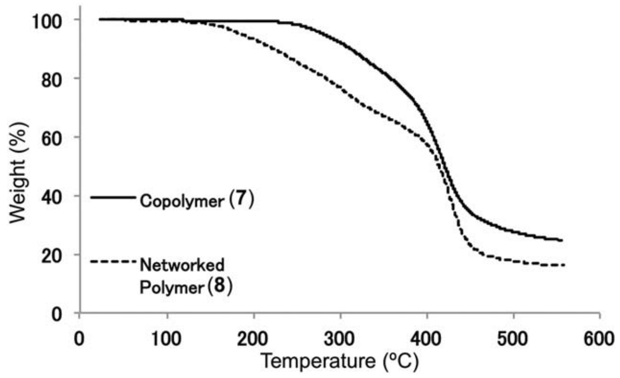


FIGURE 6 Thermogravimetric analysis of polymer **7** and **8**.

CONCLUSIONS

In this study, we described the synthesis and polymerization of 4-vinyl benzylisothiocyanate. This isothiocyanate monomer is easily synthesized by single step from commercially available 4-vinyl benzylchloride and tolerable in the presence of alcohol without any protection. In addition, this homopolymerization by conventional free-radical condition was successful, and the benzyl isothiocyanate group remained stable during conventional radical polymerization condition. The characteristic reactivity of isothiocyanate group was applicable for the copolymerization with HEMA, which is not possible for isocyanate monomer due to its harsh reactivity with alcohol. This copolymer formed networked polymer after addition of DBU.

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