Macromolecules
ARTICLE

Macromolecules **2009**, *42*, 7709–7717 **7709**
DOI: 10.1021/ma9014577

New Click Chemistry: Polymerization Based on 1,3-Dipolar Cycloaddition of a Homo Ditopic Nitrile *N*-Oxide and Transformation of the Resulting Polymers into Reactive Polymers

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Received July 5, 2009; Revised Manuscript Received September 8, 2009

ABSTRACT: Applicability and productivity of new click chemistry that exploits a nitrile *N*-oxide as a 1,3-dipole in polymer synthesis were demonstrated by the polymerization of diynes with a homo ditopic aromatic nitrile *N*-oxide. The nitrile *N*-oxide was synthesized in situ by the reaction of the corresponding hydroxamoyl chloride with molecular sieves 4 Å. The click polymerization of various ditopic diynes and the nitrile *N*-oxide efficiently produced polyisoxazoles in high yields. The homo ditopic nitrile *N*-oxide was also useful for the connection of bisacetylene-terminated polymers to give multiblock copolymers in very high yield. The resulting polyisoxazoles agree well with the structural assignment obtained by the ^{1}H and ^{13}C NMR analyses. The generated polyisoxazoles showed improved thermal stability due to the presence of isoxazole moieties. The molecular diversity of the obtained polyisoxazoles was confirmed by the selective transformations of the isoxazole moieties into β-aminoenone or β-aminoalcohol moieties with high conversion rates. The thermal decomposition temperature of the transformed polymers was lower than that of the polyisoxazoles because of the formations of abundant amino and hydroxyl groups. Furthermore, the functionality of poly(β-aminoalcohol) was proven by quantitatively cross-linking the polymers by treatment with terephthalaldehyde or methylene diphenyl diisocyanate.

Introduction

The construction of sophisticated molecular architectures requires viable, selective, and highly reliable reactions as useful synthetic tools.[1−5] Click chemistry,[6] especially the Huisgen dipolar cycloaddition of azides with alkynes, has generated particular interest as a powerful and selective method for molecular integration.[7] However, the toxicity and explosiveness of azides, in addition to the requirement of a Cu(I) catalyst, has led to limitations in the use of this method.[8] Thus, we have been exploring the potential usefulness of nitrile *N*-oxides as the substitutes for azides,[9−14] which allows efficient [2 + 3]cycloaddition with both alkenes and alkynes to selectively produce the corresponding nitrogen-containing heterocycles.[15] The cycloaddition with a nitrile *N*-oxide has been used as a powerful tool for the synthesis of diverse natural molecules,[16] because the resulting heterocycles have potential versatility in the transformations into their various derivatives, which enables simple conversion to useful functional groups such as aldol, diketone, β-aminoalcohol, and β-aminoenone. The reason why such conversions can be carried out is because the 1,3-dipolar cycloaddition using a nitrile *N*-oxide is always accompanied by C−C bond formation. This is different from the 1,3-dipolar cycloaddition using azides and acetylenes, which is the most popular click reaction used currently. The reduction of isoxazole compounds with lithium aluminum hydride was described by Unlau et al.,[17] and Torssell et al. showed that the hydrogenation of isoxazoles can selectively produce β-aminoenones or diketones, depending upon the conditions employed.[18,19] To the best of our knowledge, there is no report related to the polymer reaction of polyisoxazoles, despite versatile functionality of the isoxazoles. Thus, we envisioned that the click polymerization involving the successive conversion of the resulting isoxazole moieties would be a powerful and reliable protocol to introduce reactive points such as amino and hydroxyl groups into the polymer chain. The effective reductions of polyisoxazole could make useful polymeric derivatives containing reactive amines as a regularly repeating unit, such as poly(β-aminoenone)s or poly(β-aminoalcohol)s.[20] In general, the polyamines are important scaffolds of a variety of ion channels, vectors in gene delivery, and ion exchange resins.[21] Herein, we describe the applicability and productivity of the click polymerization exploiting a nitrile *N*-oxide based on our recent approach, as demonstrated by the polymerization of various bisalkynes with homo ditopic aromatic nitrile *N*-oxide along with simple transformation of the resulting polymers into reactive polymers.

Experimental Section

General. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded with a JEOL AL-400 NMR spectrometer using $CDCl_3$ and CD_3OD as the solvents and calibrated using residual undeuterated solvent or tetramethylsilane as the internal standard. IR spectra were recorded with a JASCO FT/IR-460 plus spectrometer. Molecular weight and molecular weight distribution were estimated by a size exclusion chromatography (SEC) with a JASCO HSS-1500 system equipped with two consecutive columns (TOSOH TSKgel GMHXL and G5000HXL; both two columns have a 9 μm of bead size with measurable molecular weight range from 1000 to 5000000) eluted with $CHCl_3$ at a flow rate of 1.0 mL/min and calibrated by polystyrene standards. The SEC profiles were recorded using a UV detector (JASCO, UV-1570) at 30 °C by a LC column oven (Chromato Science Co. Ltd., CS-600H). The decomposition temperature was obtained with a Shimadzu TGA-50 instrument at a heating rate of 10 °C/min. Differential scanning calorimetry

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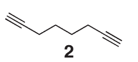
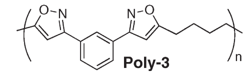
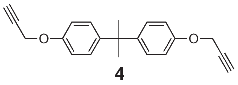
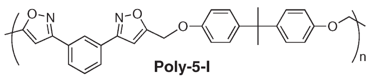
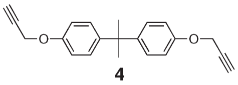
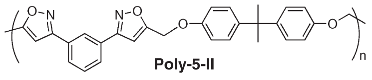
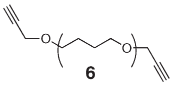
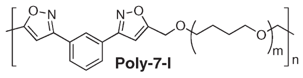
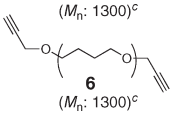
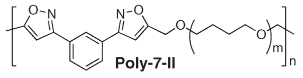
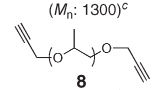
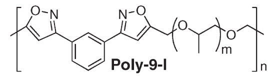
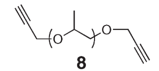
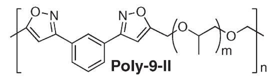
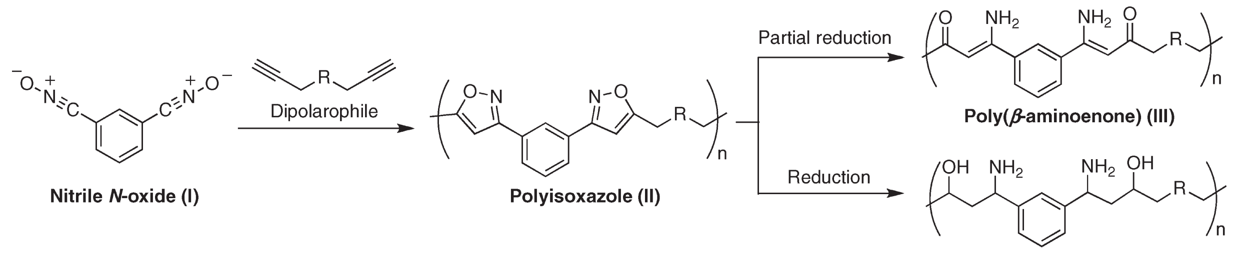
Table 1. Synthesis of Polyisoxazoles via Polycycloaddition[a,b]

Entry	Dipolarophile	Concentration / M	Products	Yield / %
1	 **2**	0.5	 **Poly-3**	84
2	 **4**	0.5	 **Poly-5-I**	78
3	 **4**	1.0	 **Poly-5-II**	85
4	 **6** (M_n: 1300)[c]	0.2	 **Poly-7-I**	78
5	 **6** (M_n: 1300)[c]	0.5	 **Poly-7-II**	98
6	 **8** (M_n: 460)[d]	0.5	 **Poly-9-I**	92
7	 **8** (M_n: 460)[d]	1.0	 **Poly-9-II**	87

[a] The hydroxamoyl chloride (**1**) was used as a precursor of the nitrile *N*-oxide. [b] Polymerization conditions: [Dipolarophile]/[**1**] = 1:1, 48 h, 80 °C, with molecular sieves 4 Å (1.6 g/mmol), in dimethylformamide (DMF). [c,d] Determined by integral ratio on ^{1}H NMR spectrum.[23]

Scheme 1. Click Polymerization Utilizing a Homo Ditopic Nitrile *N*-Oxide (I) with a Diyne and the Transformations of a Polyisoxazole (II) into Reactive Polymers (III and IV)



(DSC) was performed with a Shimadzu DSC-60 instrument at a heating rate of 10 °C/min under N_2 atmosphere at a flow rate of 50 mL/min. Thermogravimetry (TG) was performed on a Shimadzu TGA-50 instrument at a heating rate of 10 °C/min under N_2 atmosphere (flow rate 50 mL/min) to determine decomposition temperature T_{d5} at which 5% weight loss was observed.

Materials. Molecular sieves 4 Å (Wako Pure Chemicals Industries, Ltd.), palladium alumina (Pd/Al_2O_3, Wako Pure Chemicals Industries, Ltd., Pd: 5%), iron powder (Fe, Wako Pure Chemicals Industries, Ltd., 95%), and terephthalaldehyde (TPA, Wako Pure Chemicals Industries, Ltd., 95%) were directly used as received. Ammonium chloride (Nacalai Tesque, Inc., 99.0%) was used as received. Commercial grade 4,4′-methylenebis(phenyl isocyanate) (methylene diphenyl diisocyanate; MDI, 98%, Tokyo Chemical Industry Co. Ltd.) was distilled under reduced pressure before use. Other commercially available solvents and reagents were directly used without further purifications except as noted below.

Typical Procedure for Click Polymerization. (i) A typical experimental procedure for the reaction of 1,3-(dicarbohydroxamoyl dichloro)benzene **1**[9] and 4,4′-(propane-2,2-diyl)bis((prop-2-ynyloxy)benzene) **4** is as follows. Benzene-1,3- dicarbohydroxamoyl dichloride **1** was prepared according to our previous report.[9] Molecular sieves 4 Å (4.2 g) was added to a solution of **1** (611 mg, 2.62 mmol) and **4** (800 mg, 2.62 mmol) in dimethylformaldehyde (DMF; 5.2 mL) at room temperature. The resulting slurry was stirred at room temperature for 30 min and at 80 °C for 24 h. The mixture was dissolved in $CHCl_3$ and filtered, and the filtrate was precipitated into MeOH. The precipitates were collected by filtration and dried in vacuo to give 4,4′-(propane)bis((prop-2-ynyloxy)benzene)-containing polyisoxazole **poly-5-I** (1.02 g, 78.5%) as a pale yellow powder. **Poly-5-I**: M_w 11700; M_n 6600; M_w/M_n 1.8 (estimated by SEC); glass transition temperature (T_g) 108.4 °C; 5% weight loss temperatures (T_{d5}) 334 °C; 10% weight loss temperatures (T_{d10}) 358 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ 8.21 (brd, 1 H), 7.88 (brd, 2 H), 7.53 (brd, 1 H), 7.15 (brd, 4 H), 6.88 (brd, 4 H), 6.69 (brd, 2 H), 5.12 (brd, 4 H), 1.63 (brd, 6 H) ppm; ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ 169.0, 161.9, 155.6, 144.1, 129.5, 128.4, 127.9, 127.7, 125.1, 114.1, 101.3, 61.4, 41.8, 30.9 ppm; IR (KBr) ν 3127 (C−H, aromatic), 2930 (C−H, str, asym), 2871 (C−H, str, sym), 1241 (phenyl−O−CH_2, str) cm^{-1}.

The alkylene spacer-containing polyisoxazole **poly-3** was obtained by the polymerization of **1** with 1,7-octadiyne **2** to give according to the same procedure (Table 1, entry 1). In addition, the polymerization of **1** with **4** to give the corresponding polyisoxazole **poly-5-II** according to the same procedure, except for the concentration (1.0 M) of **1** (Table 1, entry 3).

(ii) A typical procedure for the reaction of **1** and bisacetylene-terminated polytetrahydrofuran (**6**) is as follows. Molecular sieves 4 Å (686 mg) was added to a solution of **1** (100 mg, 0.43 mmol) and **6** (463 mg, 0.43 mmol) in DMF (2.1 mL) at room temperature. The resulting slurry was stirred at room temperature for 30 min and at 80 °C for 24 h. The mixture diluted with $CHCl_3$ was filtered and the filtrate was precipitated into MeOH. The precipitates were collected by filtration and dried in vacuo to give polytetrahydrofurane-containing polyisoxazole **poly-7-I** (415 mg, 78.1%) as a yellow elastomer. **Poly-7-I**: M_w 71400; M_n 34700; M_w/M_n 2.0 (estimated by SEC); T_g −66.2 °C; T_{d5} 327 °C; T_{d10} 357 °C; ^1H NMR (298 K, $CDCl_3$) δ 8.23 (brd, 1 H), 7.90 (brd, 2 H), 7.55 (brd, 1 H), 6.61 (brd, 2 H), 4.64 (brd, 4 H), 3.61−3.58 (m, terminal $O-CH_2$), 3.41 (brd, 4 H), 1.61 (brd, 4 H) ppm; ^{13}C NMR (400 MHz, 298 K, $CDCl_3$) δ 170.5, 161.7, 129.7, 129.5, 128.2, 125.2, 100.8, 71.2, 70.5−70.3, 26.4−26.3 ppm; IR (NaCl) ν 3122 (C−H, aromatic), 2941 (C−H, str, asym), 2852 (C−H, str, sym), 1119 (CH_2-O-CH_2, str) cm^{-1}.

Polytetrahydrofuran-containing polyisoxazole **poly-7-II** was obtained by the polymerization of **1** with bisacetylene-terminated polytetrahydrofuran (**6**) according to the same procedure except for the concentration (0.5 M) of **1** (Table 1, entry 5). Polypropyleneoxide-containing polyisoxazole **poly-9-I** and **poly-9-II** were obtained by the polymerization of **1** with bisacetylene-terminated polypropyleneoxide **8** according to the same procedure except for the concentration (0.5 and 1.0 M) of **1** (Table 1, entries 6 and 7).

Selective Reduction. Typical procedures for the selective reduction of polyisoxazoles are as follows:

(i) A DMF solution of **poly-3** (30 mg/300 μL) was added to Pd/Al_2O_3 (50 mg). The atmosphere was replaced with H_2 (g) and the resulting mixture was stirred at 80 °C for 24 h. The reaction mixture was filtered through a Celite pad and washed with MeOH. The organic solution was evaporated to give alkylene spacer-containing poly(β-aminoenone) **poly-3a** as a yellow solid (21 mg, 69%). IR (KBr) ν 3422 (NH_2, str), 1707 (β-unsaturated ketones), 1524 (NH_2, bend) cm^{-1}.

(ii) Ammonium chloride (856 mg, 16.0 mmol) and Fe powder (894 mg, 16.0 mmol) were added to a solution of the **poly-5-I** (400 mg, 0.80 mmol/unit) in DMF/MeOH (4 mL, DMF/MeOH = 5:1). The mixture was stirred at 110 °C for 3 days. The crude mixture was precipitated into water. The precipitates were stirred with activated charcoal in ethanol for 3 h under reflux. The mixture was filtered through a Celite pad and concentrated in vacuo to give the corresponding poly(β-aminoenone) **poly-5a** as a yellow solid (336 mg, 84%). T_g 54.1 °C; T_{d5} 229 °C; T_{d10} 261 °C; ^1H NMR (400 MHz, 298 K, $CDCl_3$) δ 10.1 (brd, NH_2), 8.10−8.03 (m, 1 H), 7.71 (brd, 1 H), 7.60 (brd, 2 H), 7.12 (s, 4 H), 6.81 (s, 4 H), 5.87 (brd, 2 H), 4.55 (brd, 4 H), 1.61 (s, 6 H) ppm. IR (KBr) ν: 3468 (NH_2, str), 1684 (β-unsaturated ketones), 1614 (NH_2, bend), 648 (NH_2, bend) cm^{-1}.

(iii) A solution of the **poly-5-I** (30 mg, 0.06 mmol/unit) in tetrahydrofuran (THF, 2.0 mL) was added to a suspension of $LiAlH_4$ (50.1 mg, 1.32 mmol) in THF (1.0 mL) at 0 °C under an Ar atmosphere. The mixture was refluxed for 24 h, cooled to 0 °C, and quenched by adding of satd aq Na_2SO_4. The precipitates were removed by filtration. The filtrate was evaporated and dried in vacuo to give the corresponding poly(β-aminoalcohol) **poly-5b** as a yellow solid (23.0 mg, 77%). T_g 10.9 °C; T_{d5} 252 °C; T_{d10} 286 °C; ^1H NMR (400 MHz, 298 K, CD_3OD) δ 7.14 (brd, 1 H), 6.99 (brd, 2 H), 6.88−6.85 (m, 4 H), 6.71 (brd, 1 H), 6.52−6.50 (m, 4 H), 4.48 (brd, H), 3.91−3.62 (m, H), 1.49−1.45 (m, 6 H) ppm; ^{13}C NMR (100 MHz, 298 K, CD_3OD) δ 161.5, 157.9, 142.4, 128.7, 128.6, 116.4, 116.2, 114.9, 62.8, 42.5, 42.3, 31.8, 31.7, 30.1 ppm; IR (KBr) ν 3396 (NH_2, str), 3304 (OH, hydrogen bonded), 1655 (NH_2, bend), 830 (NH_2, bend) cm^{-1}.

(iv) Polytetrahydrofurane-containing poly(β-aminoalcohol) **poly-7b**: A solution of the **poly-7-I** (100 mg, 80.0 μmol/unit) in THF (2.0 mL) was added to a suspension of $LiAlH_4$ (106 mg, 2.80 mmol) in THF (2.0 mL) at 0 °C under an Ar atmosphere. The mixture was refluxed for 24 h, cooled to 0 °C, and quenched by adding of satd aq Na_2SO_4. The precipitates were removed by filtration. The filtrate was evaporated and dried in vacuo to give **poly-7b** as a yellow oil (98.0 mg, 98%). T_g −92.6 °C; T_{d5} 298 °C; T_{d10} 349 °C; IR (KBr) ν 3418 (NH_2, str, OH, hydrogen bonded), 1523 (NH_2, bend), 881 (NH_2, bend) cm^{-1}.

Synthesis of Network Polymers. Typical procedures for cross-linked gel formation of poly(β-aminoalcohol)s are as follows:

(i) Network polymer (**MDI-7b**) prepared from **poly-7b** with MDI: **Poly-7b** (100 mg, 80.0 μmol/unit) was dissolved in DMF (300 μL). Methylene diphenyl isocyanate (MDI; 20.0 mg, 80.0 μmol) was added to the solution. The solution was stirred at room temperature. After 30 min, the obtained gel (**MDI-7b**) was washed with $CHCl_3$ and dried in vacuo to give the xerogel (120 mg) in a quantitative yield. T_g −61.9 °C; T_{d5} 280 °C; T_{d10} 304 °C; IR (KBr) ν 1727 (C=O), 1705 (amide), 1657 (ureas) cm^{-1}.

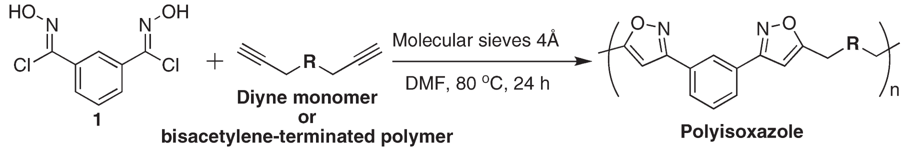
(ii) Network polymer (**MDI-8b**) prepared from **poly-8b** with MDI: The network gel formation of **poly-8b** was carried out in the same manner. Yield: 98%; T_g −14.8 °C; T_{d5} 166 °C; T_{d10} 214 °C; IR (KBr) ν 1732 (C=O), 1704 (amide), 1658 (ureas) cm^{-1}.

Table 2. Molecular Weight and Thermal Properties of the Polyisoxazoles

polyisoxazole	M_w[a]	M_n[a]	M_w/M_n[a]	T_g[b] (°C)	T_{d5}[c] (°C)	T_{d10}[c] (°C)
Poly-3	2300	1400	1.6	48.1	310	342
Poly-5-I	11700	6600	1.8	108.4	334	358
Poly-5-II	9200	4900	1.9	[d]	[d]	[d]
Poly-7-I	71400	34700	2.0	−66.2	327	357
Poly-7-II	419300	74300	5.6	[d]	[d]	[d]
Poly-9-I	8500	5400	1.6	[d]	[d]	[d]
Poly-9-II	14200	5500	2.6	−27.3	274	290

[a] M_n: number average molecular weight; M_w: weight average molecular weight were estimated by size exclusion chromatography ($CHCl_3$, on the basis of polystyrene standards). [b] Glass transition temperatures (T_g) were obtained at a heating rate of 10 °C/min under N_2 (flow rate 50 mL/min) in the scan. [c] 5% (T_{d5}) and 10% (T_{d10}) weight loss temperatures were obtained at a heating rate of 10 °C/min under N_2 (flow rate 50 mL/min). [d] Not estimated.

Scheme 2. Synthesis of Polyisoxazoles Using 1 as a Precursor to Nitrile *N*-Oxide with Diynes[a]



1

Diyne monomer
or
bisacetylene-terminated polymer

Polyisoxazole

[a] DMF: dimethylformamide.

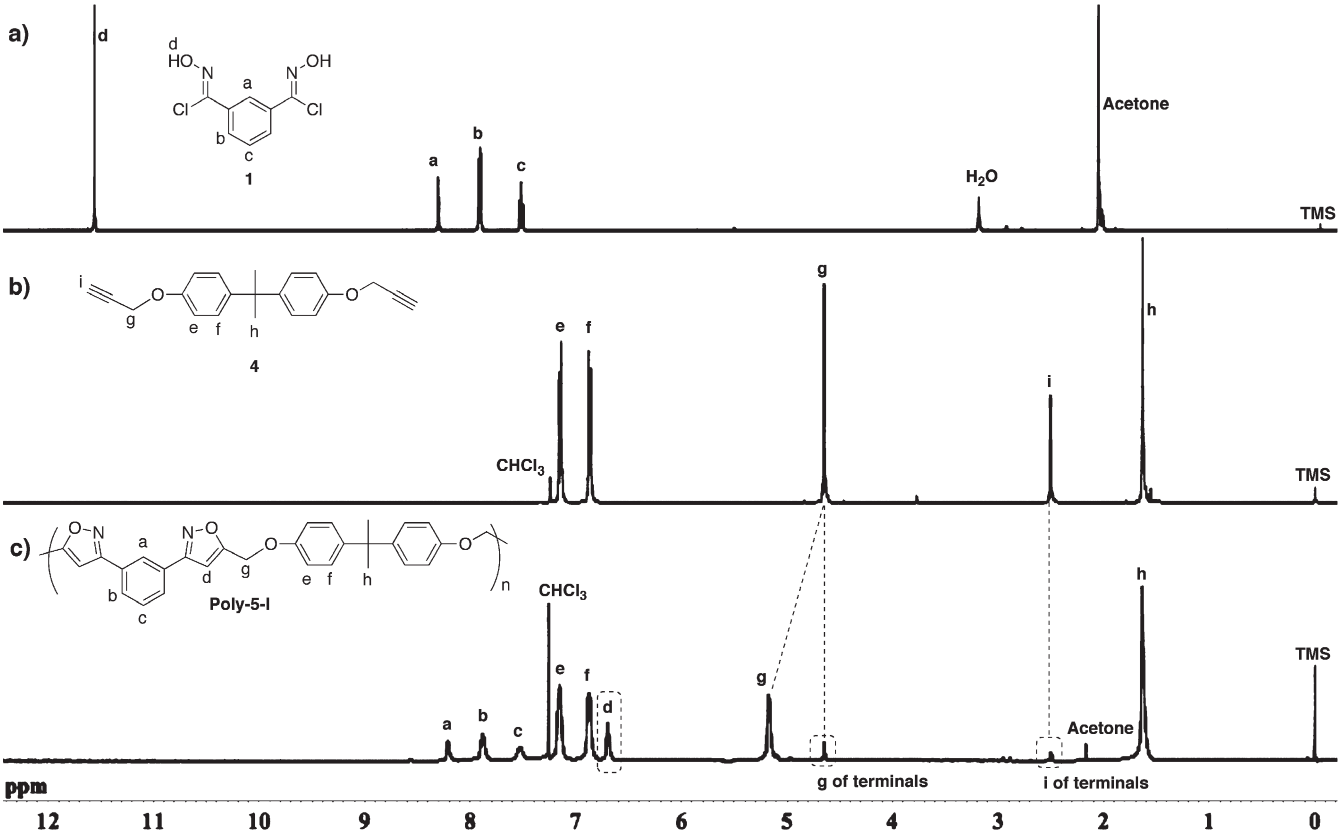
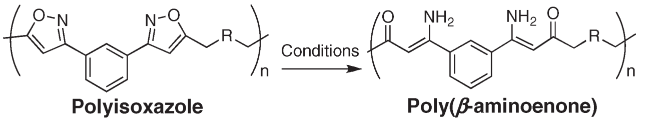
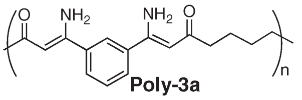
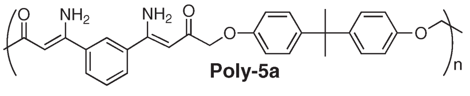


Figure 1. ^{1}H NMR spectra (400 MHz, 298 K) of (a) **1** ($(CD_3)_2CO$), (b) 4,4′-(propane-2,2-diyl)bis((prop-2-ynyloxy)benzene) **4** ($CDCl_3$), and (c) **poly-5-I** ($CDCl_3$).

Table 3. Reduction of the Polyisoxazoles under Various Conditions



Entry	Polyisoxazole	Reducing agent	Solvent	Temp. (°C)	Time (h)	Product	Yield (%)
1	**Poly-3**	Zn[a]	DMF/H_2O	80	12	–[e]	–[f]
2	**Poly-3**	Zn[a]	AcOH	80	24	–[e]	–[f]
3	**Poly-3**	$RhCl(PPh_3)_3$[b], H_2 (g)	CH_2Cl_2/AcOH	25	12	–[e]	–[f]
4	**Poly-3**	Pd/Al_2O_3[c], H_2 (g)	DMF	80	12	 **Poly-3a**	69
5	**Poly-5-I**	Pd/Al_2O_3[c], H_2 (g)	DMF	80	12	Complex mixture	–[g]
6	**Poly-5-I**	Fe[d], NH_4Cl	DMF/MeOH	80	72	 **Poly-5a**	84

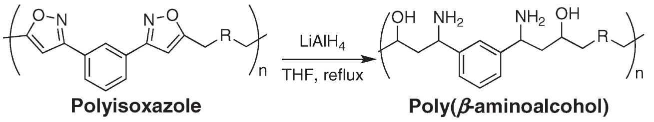
[a] Zinc powder (30.6 equiv/unit). [b] $RuCl(PPh_3)_3$ (20 mol %/unit). [c] Pd/Al_2O_3 (62.5 wt %). [d] Fe powder (20 equiv/unit) and ammonium chloride (20 equiv/unit) were used. [e] No reaction. [f] Starting material was recovered quantitatively. [g] Not estimated. Ph = phenyl, DMF = dimethylformamide, Ac = acetyl, Me = methyl.

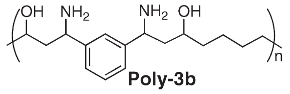
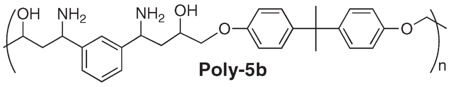
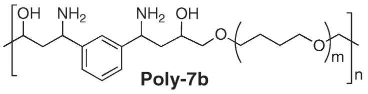
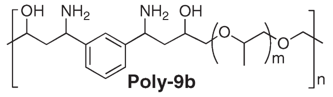
(iii) Network polymer (**TPA-5b**) prepared from **poly-5b** with TPA: Terephthalaldehyde (TPA; 8.0 mg, 60 μmol) was added to a solution of **poly-5b** (30 mg, 60 μmol/unit) in DMF (125 μL) at room temperature. The solution was warmed to 80 °C and stirred for 24 h. The obtained gel (**TPA-5b**) was washed with $CHCl_3$ and dried in vacuo to give the xerogel in a quantitative yield. T_g 21.4 °C; T_{d5} 170 °C; T_{d10} 208 °C; IR (KBr) *ν* 1700 (Aryl-CHO), 1654 (C=N, imine) cm^{-1}.

Results and Discussion

Synthesis of Polyisoxazoles by Click Polymerization and their Properties. Scheme 1 shows the general strategy of

Table 4. Selective Reduction of the Polyisoxazoles with $LiAlH_4$



Entry	Polyisoxazole	Time (h)	Product	Yield (%)
1[a]	**Poly-3-I**	12	 **Poly-3b**	86
2[a]	**Poly-5-I**	12	 **Poly-5b**	77
3[b]	**Poly-7-I**	12	 **Poly-7b**	98
4[b]	**Poly-9-II**	12	 **Poly-9b**	81

[a] $LiAlH_4$ (15 equiv/unit). [b] $LiAlH_4$ (23 equiv/unit).

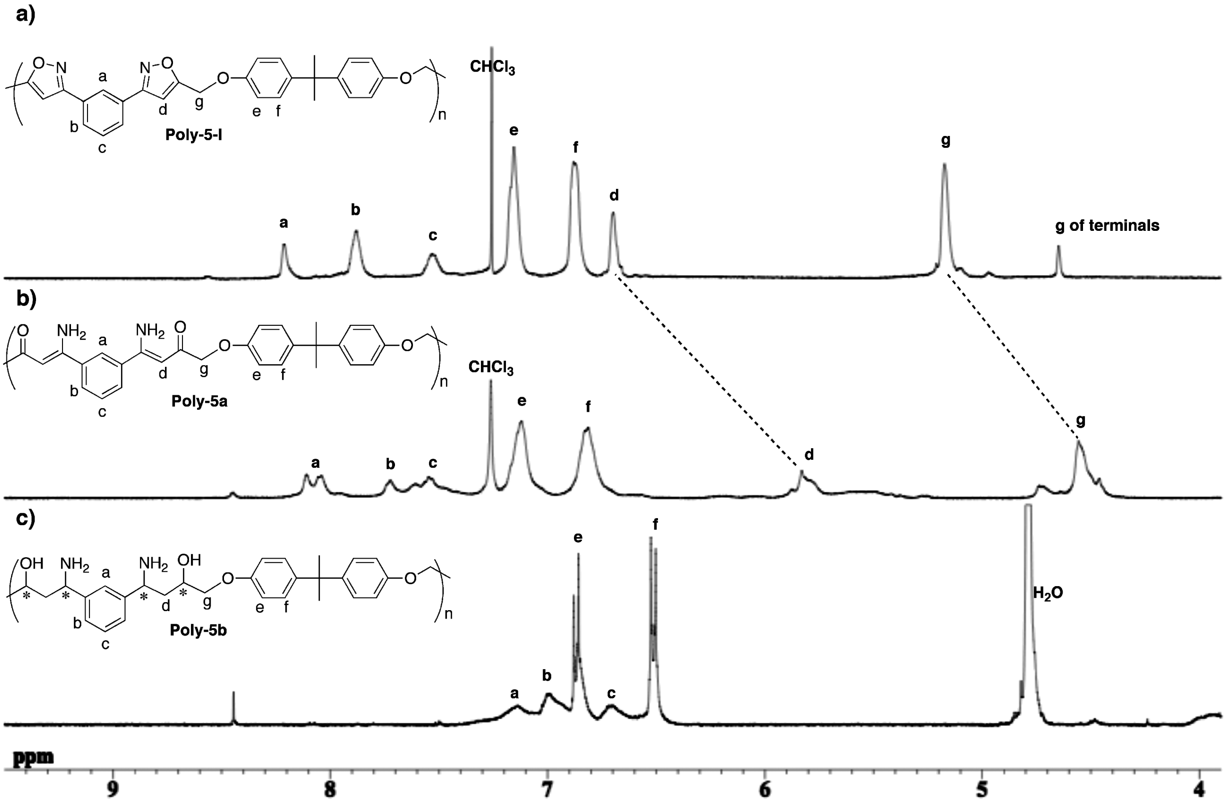
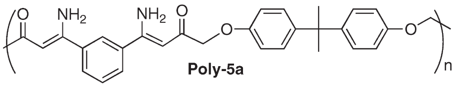
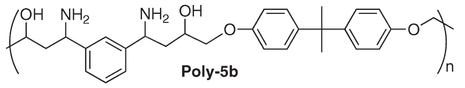
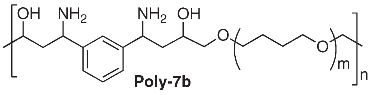
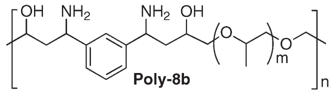


Figure 2. Partial ^1H NMR spectra (400 MHz, 298 K) of (a) **poly-5-I** ($CDCl_3$), (b) **poly-5a** ($CDCl_3$), and (c) **poly-5b** (CD_3OD).

the click polymerization using homo ditopic nitrile *N*-oxide and the successive conversion of the resulting polymer into reactive polymers.[22] The nitrile *N*-oxide (I) is generated in situ from a bifunctional chloroxime (**1**) as the precursor.[9] Polyisoxazole (II) is obtained by the polycycloaddition of 1,3-bis(nitrile *N*-oxide)benzene (I) with diynes. While the selective N−O bond cleavage of the isoxazole moiety in the resulting polyisoxazole (II) would afford poly(β-aminoenone)s (III), the complete reduction of the isoxazole moiety affords a poly(β-aminoalcohol) (IV).

Table 5. Thermal Properties of Poly(*β*-aminoenone) and Poly(*β*-aminoalcohol)s

Product	T_g [a] (°C)	T_{d5} [b] (°C)	T_{d10} [b] (°C)
 **Poly-5a**	54.1	229	261
 **Poly-5b**	10.9	252	286
 **Poly-7b**	−92.6	298	349
 **Poly-8b**	−60.3	156	195

[a] Glass transition temperatures were obtained at a heating rate of 10 °C/min under nitrogen (flow rate 50 mL/min) in the scan. [b] 5% and 10% weight loss temperatures were obtained at a heating rate of 10 °C/min under nitrogen (flow rate 50 mL/min).

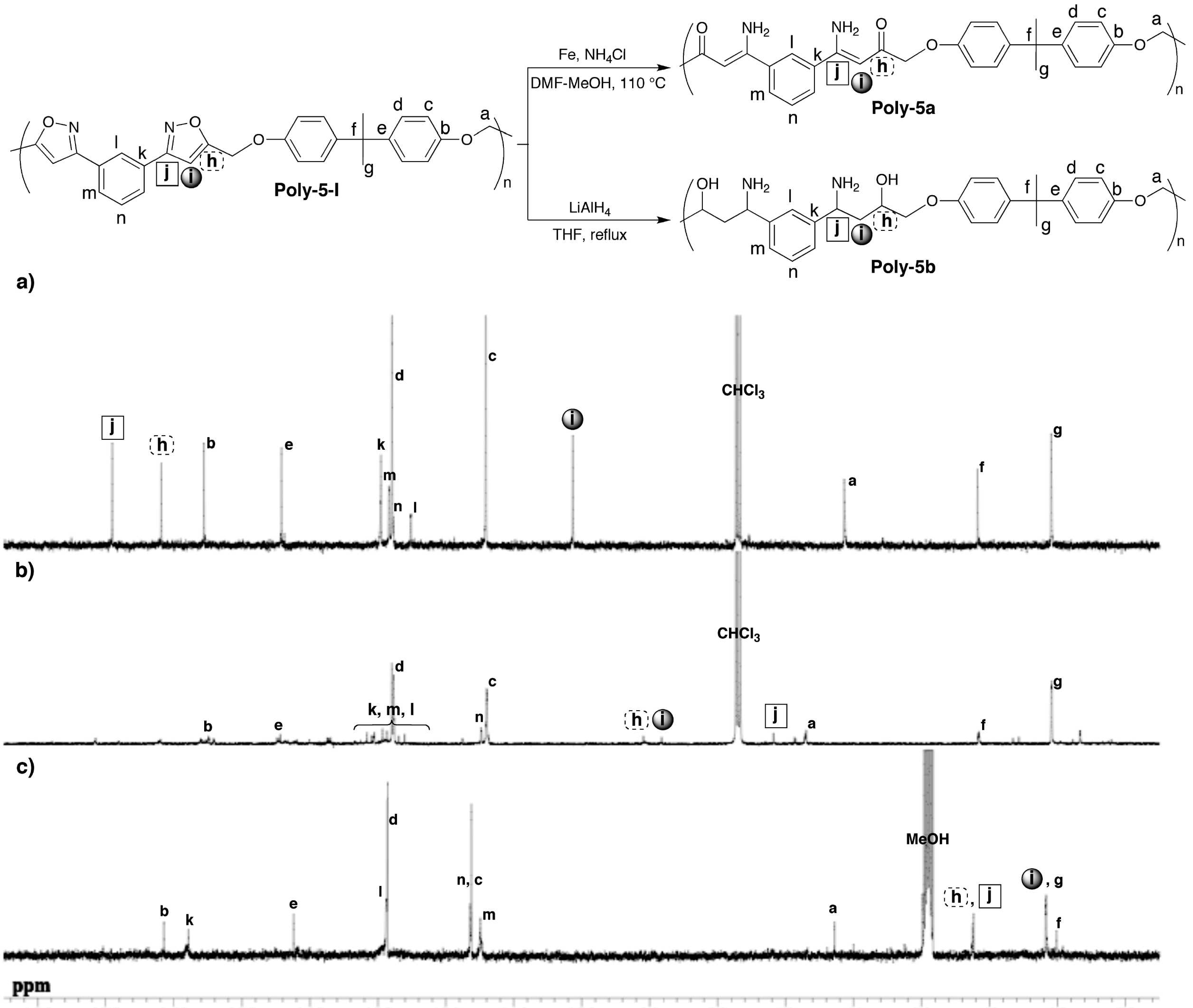
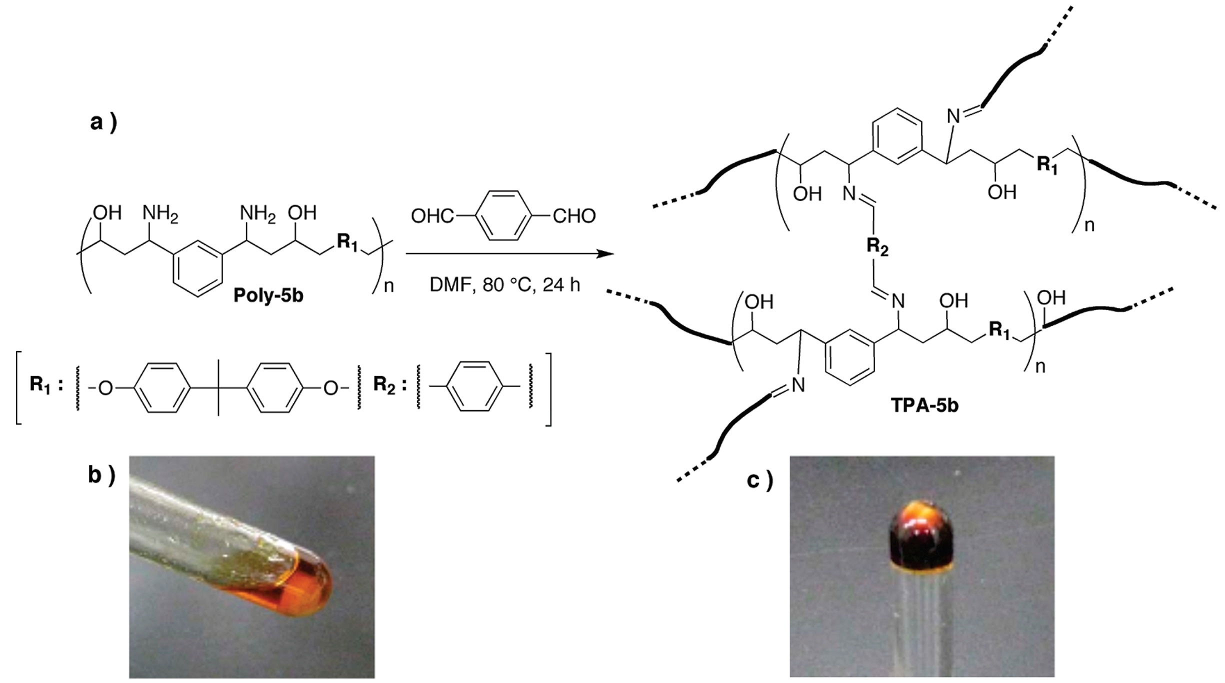


Figure 3. ^{13}C NMR spectra (100 MHz, 298 K) of (a) **poly-5-I** ($CDCl_3$), (b) **poly-5a** ($CDCl_3$), and (c) **poly-5b** (CD_3OD).

In the actual experiments, several bifunctional terminal acetylenic monomers (**2** and **4**) and bisacetylene-terminated polymers (**6** and **8**) were employed to prove the usefulness of the click polymerization. The results are summarized in Tables 1 and 2.

Scheme 3. (a) Schematic Representation of the Network Formation from poly-5b and Terephthalaldehyde; (b) Photograph of a poly-5b Solution in DMF (240 g/L); (c) Photograph of TPA-5b



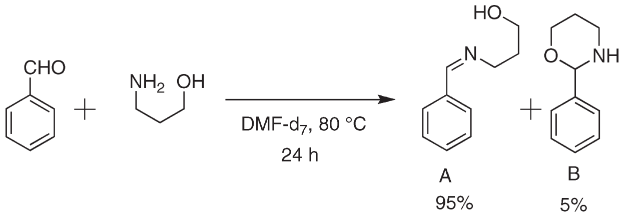
For example, the polymerizations of 1,7-octadiyne (**2**) and 4,4′-(propane-2,2-diyl)bis(ethynyloxybenzene) (**4**) with **1** in the presence of molecular sieves 4 Å in DMF at 80 °C proceeded well to afford the corresponding polyisoxazoles **poly-3**, **poly-5-I**, and **poly-5-II** in very high yields (Scheme 2; Table 1, entries 1−3).[23]

While **poly-3** had a low molecular weight (M_n 1600), **poly-5-I** had a higher molecular weight (M_n 6600) and was obtained when bisphenol A-based monomer **4** reacted with **1**. The difference in molecular weight was probably due to the higher solubility of **poly-5-I** in DMF compared with that of **poly-3** (Table 2). The concentration of **4** did not significantly affect the polymerization. (Table 2, **poly-5-I**: M_n 6600; **poly-5-II**: M_n 4900). In addition, we discovered that this polycycloaddition can be applied not only to low molecular weight monomers but also to high molecular weight monomers such as diacetylene-terminated polytetrahydrofuran (**6**) and polypropylene glycol (**8**; Table 1, entries 4−7). Treatment of **6** and **8** with **1** under similar conditions afforded the corresponding polyisoxazoles that possessed block copolymer structures of high molecular weights and yields (Table 2, **poly-7-I**: M_n 34700; **poly-9-II**: M_n 5500).

The thermal properties of the polymers were evaluated by DSC and TGA (Table 2). The glass transition temperature (T_g) appeared in the range from −66 to 108 °C, clearly depending on the spacer structures of the diyne monomers. The thermal weight loss temperatures of **poly-3-I** and **poly-5-I** (T_{d5} and T_{d10}) were observed in the range 310−358 °C, indicating the thermal stability of the isoxazole skeleton. The T_{d10} of **poly-7-I** (357 °C) and **poly-9-II** (290 °C) were higher than the reported T_{d10} of polytetrahydrofurane (310 °C) and polypropylene glycol (250 °C), suggesting the increased thermal stability due to the isoxazole moieties.[24]

The structures of the polyisoxazoles were determined by ^1H and ^{13}C NMR analyses. Representative examples of ^1H and ^{13}C NMR spectra are shown in Figures 1 and 3.[23] As shown in Figure 1, the new characteristic signals of heteroaromatic protons at 6.69 ppm (**d**) and benzyl protons at 5.12 ppm (**g**) were observed in the spectrum of **poly-5-I**. The downfield shift of the benzyl proton signal **g** of **4** and significant reduction of the ethynyl proton signal **i** of **4** along with the disappearance of the OH signal **d** of **1** clearly suggested the formation of **poly-5-I**. The carbon signals at 169.0 (**j**), 161.9 (**h**), and 101.3 (**i**) ppm were also assigned as those of the isoxazole moiety in the ^{13}C NMR spectrum of **poly-5-I** (Figure 3a). Other carbon signals of **poly-5-I** agree well with its structure.

Scheme 4. Model Reaction of Benzaldehyde with 3-Aminopropanol[23]



Modification of Polyisoxazoles. The simple transformation of the isoxazole moieties was carried out using reducing agents. Table 3 summarizes the results of experiments conducted with two polyisoxazoles under various conditions. Treatment of **poly-3** with Pd/Al_2O_3 as the catalyst of hydrogenation under H_2 gas and treatment of **poly-5-I** with excess amount of Fe(0) in the presence of NH_4Cl as the reducing agent perfectly converted the polyisoxazoles to the corresponding poly(β-aminoenone)s in high yields (Table 3, entries 4 and 6).[25] On the other hand, the use of Pd/Al_2O_3 under H_2 gas with **poly-5-I** did not produce the desired result (entry 5), probably owing to the reductive cleavage of the benzyl C−O bond as a side reaction.[26] The β-aminoenone moieties of **poly-5a** showed some characteristic resonances in ^1H NMR, ^{13}C NMR, and IR spectra.

Alternative synthesis of reactive polymers from polyisoxazoles was examined as shown in Table 4. The polyisoxazoles were completely transformed to poly(β-aminoalcohol)s in 77−98% yields by reduction with $LiAlH_4$. Both **poly-7-I** and **poly-9-II** were similarly transformed into **poly-7b** and **poly-8b**, respectively, by the $LiAlH_4$ reduction.

Scheme 5. (a) Schematic Representation of the Network Formation from the Poly(*β*-aminoalcohol) and MDI; (b) Photograph of a DMF Solution of poly-7b (33 g/L); (c) Photograph of MDI-7b

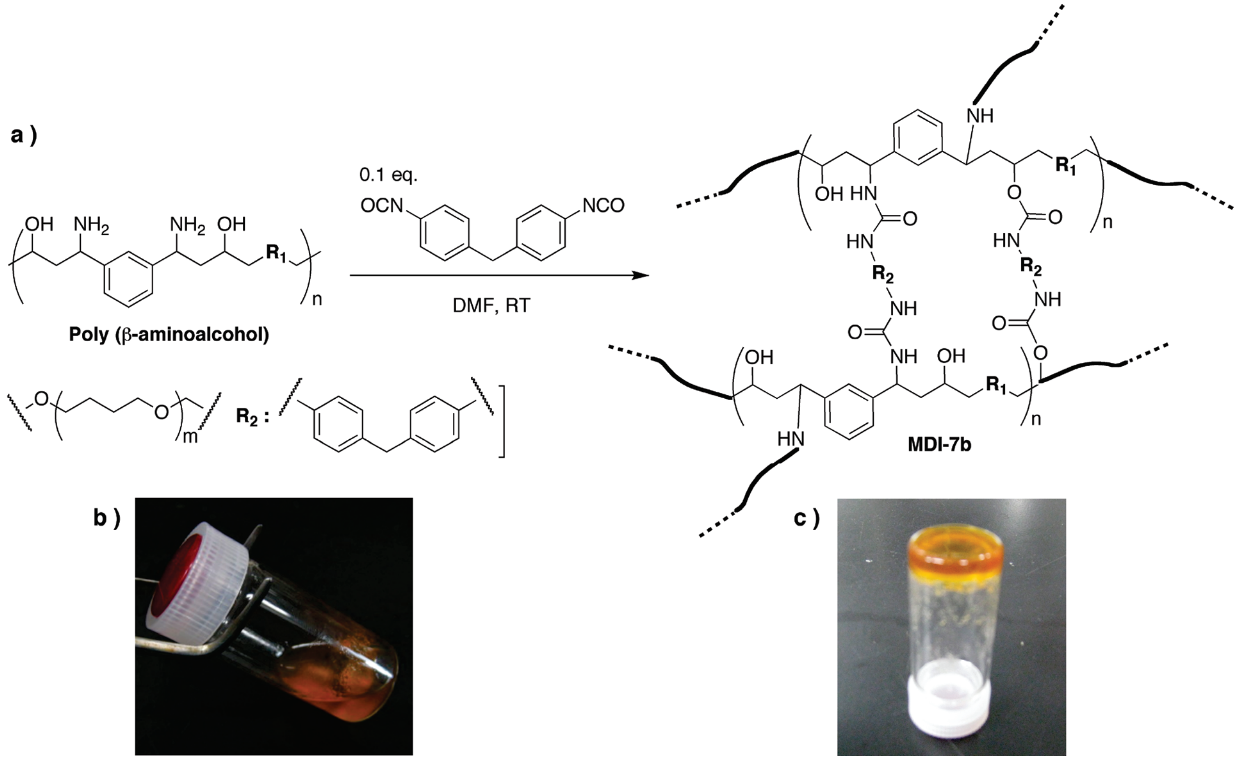


Figure 2 shows the ^{1}H NMR spectra of the reactive polymers. The signals of heteroaromatic protons (**d**) at 6.69 ppm and benzyl protons (**g**) at 5.12 ppm of **poly5-I** disappeared after reduction, whereas the olefinic signals (**d**) at 5.83 ppm and ether methylene signals (**g**) at 4.55−4.66 ppm appeared after reduction, as shown in Figure 2b.

Broad carbon signals observed in ^{13}C NMR spectrum of **poly-5a** (Figure 3b) might be derived from the presence of tautomers of the aminoenone moieties.[27] Although, the heteroaromatic carbon signals (169.0, 161.9, and 101.3 ppm, Figure 3a) in the ^{13}C NMR spectrum of **poly-5-I** were not seen in that of **poly-5a** (Figure 3b), the spectra of **poly-5a** is complicated and prevent complete assignment. The IR spectrum of **poly-5a** exhibited the characteristic absorption bands in the region of primary amine at 3468, 1614, and 648 cm^{-1}, all of which are due to the amine stretching modes.[23] In addition, **poly-5a** showed an absorption band in the region of a *β*-unsaturated carbonyl (1684 cm^{-1}) corresponding to *β*-enone carbonyl stretching modes.[23] These spectral changes strongly support the structural change of **poly-5-I** to **poly-5a**.

Poly-5-I was clearly transformed into **poly-5b** in 77% yield (Table 4, entry 2). **Poly-5b** also showed too broad proton signals assigned to methylene groups (**d**, **g**). These broaden signals are indicative of diastereomeric structures such as **poly-5b**, which contains four chiral carbons (Figure 2c). On the other hand, the sharp aromatic carbon signals of **poly-5-I** decreased together with the disappearance of the heteroaromatic carbon signals (169.0, 161.9, and 101.3 ppm) and the appearance of the aliphatic carbon signals (42.5, 42.3, and 31.8 ppm, Figure 3a,c). This spectral change was consistent with the structural change of **poly-5-I** to **poly-5b**. Moreover, **poly-5b** showed IR absorption bands indicative of primary amine (3396 cm^{-1}) and hydroxyl groups (3304 cm^{-1}), both of which are assignable to the *β*-aminoalcohol structure.[23] From these results, the reduction of **poly-5-I** with $LiAlH_4$ clearly gave poly(*β*-aminoalcohol) **poly-5b**. Thus, efficient reactions of the polyisoxazoles were successfully conducted to yield poly(*β*-aminoalcohol) reactive polymers.

The solubility differences between **poly-5-I** and **poly-5b** were also confirmed. **Poly-5b** is not soluble in less polar solvents such as $CHCl_3$ and CH_2Cl_2 but is soluble in polar solvents such as CH_3OH; **poly-5-I** is not soluble in CH_3OH. Thermal properties of the obtained polymers are summarized in Table 5. The lowered T_g of poly(*β*-aminoalcohol)s in comparison with polyisoxazoles clearly corresponds to the structural change, that is, the increased flexibility of the polymer chain of poly(*β*-aminoalcohol)s by decomposition of the heteroaromatic moieties. The thermal decomposition temperature of the reduced polymers was lower than that of the polyisoxazoles due to the formations of amino and hydroxyl groups.

Synthesis of Network Polymers using Poly(*β*-aminoalcohol). The utility of poly(*β*-aminoalcohol)s was demonstrated through the simple conversion to network polymers with a typical cross-linker such as TPA or MDI. On the basis of our preliminary study, the synthesis of a network polymer using **poly-5b** and TPA was carried out. Scheme 3 shows that treatment of **poly-5b** with TPA in DMF for 24 h at 80 °C afforded a gelled product (**TPA-5b**). The gel was washed with $CHCl_3$ and dried in vacuo to give a xerogel in a quantitative yield. The characteristic IR absorptions of the imine (1654 cm^{-1}) and aromatic aldehyde (1700 cm^{-1}) of the xerogel are consistent with the formation of **TPA-5b**.[23]

Because the formation of both imine and cyclic 1,3-oxazinane structures by the treatment of **poly-5b** with TPA was possible, the model reaction using benzaldehyde and 3-aminopropanol was examined in DMF at 80 °C (Scheme 4). As a result, 2-phenyl-1,3-oxazinane B was obtained as a minor product (5%), along with the imine compound A (95%). This result suggested that the cross-linking mostly occurred via imine bond formation.[23]

The cross-linking reaction of polytetrahydrofuran-containing poly(β-aminoalcohol) **poly-7b** was performed with MDI (0.1 equiv) in DMF at room temperature to quantitatively yield a transparent gelled product (**MDI-7b**) within 3 h (Scheme 5). The IR spectrum of **MDI-7b** showed the absorptions based on the carbonyl stretching vibration of not only the urea group (1657 cm^{-1}) but also the urethane group (1720 and 1705 cm^{-1}).[23] The absorptions of the two carbonyl groups strongly suggest that both amino and hydroxy groups participate into the cross-linking. Thus, the usefulness of poly(β-aminoalcohol)s as a reactive polymer was demonstrated.

Conclusions

Our results have shown the applicability and productivity of new click polymerization reactions that exploit a homo ditopic nitrile *N*-oxide as a bifunctional 1,3-dipole formed in situ from the corresponding bifunctional hydroxamoyl chloride. The polycycloadditions with various dialkynes including polymeric dialkynes proceeded to give high yields of polyisoxazoles. The molecular diversity of the polyisoxazoles was confirmed by the simple conversions to poly(β-aminoenone)s and poly(β-aminoalcohol)s as the reactive polymers, both of which underwent efficient gelation by reaction with typical cross-linkers. These click polymerization reactions can be characterized by the following positive traits: (i) no-explosive materials were involved, (ii) the versatility of dipolarophiles used (both dialkyne and dialkene are available although the present paper only dealt with dialkynes), (iii) the reaction included C−C bond formation, (iv) these are catalyst-free systems, and (v) possible transformation of the resulting polymers. Thus, the present new click polymerization using homo ditopic diynes and a nitrile *N*-oxide including the facile transformation of the resulting polyisoxazoles into the reactive polymers would be a useful synthetic entry of new polymers. Further studies of click polymerization are currently in progress.

Acknowledgment. This work was partially supported by the Global COE program (Tokyo Institute of Technology), a Grant-in-Aid for Scientific Research (JSPS), and Mizuho Foundation for the Promotion of Science.

Supporting Information Available: Experimental details, ^{1}H and ^{13}C NMR spectra, and IR chart. This material is available free of charge via the Internet at http://pubs.acs.org.

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