Synthesis of Ordered Polymer by Direct Polycondensation. 9. Ordered Poly(amide−acylhydrazide−amide) from Three Nonsymmetric Monomers

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ABSTRACT: An ordered (−ccfebaddabef−) poly(amide−acylhydrazide−amide) was prepared by the direct polycondensation of 5-(3-carboxypropyl)-2-isopropoxybenzoic acid (XabX), bis(4-nitrophenyl) isophthalate (XccX), piperazine (YddY), and 4-aminobenzohydrazide (YefY), using the condensing agent diphenyl(2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (**1**). The polymerization was carried out by mixing the dicarboxylic acid, diester, condensing agent **1**, and triethylamine (TEA) in *N*-methyl-2-pyrrolidinone (NMP) for 3 h at room temperature, followed by adding piperazine and aminobenzohydrazide at −15 °C. The mixture was stirred at −15 °C for 2 h, room temperature for 24 h, and 70 °C for 4 d in the presence of 1-hydroxybenzotriazole (HOBt). The resulting polymer gave an inherent viscosity of 0.20 dL/g in NMP, measured at a concentration of 0.5 g/dL at 30 °C. The feasibility of the formation of the ordered polymer from three nonsymmetric monomers was demonstrated by studying the model reactions in detail. Furthermore, the authentic ordered and random polymers were prepared to verify the structure of the ordered polymer. The microstructures of the polymers obtained were investigated by ^{1}H and ^{13}C NMR spectroscopy, and it was found that the polymer obtained by direct polycondensation has the expected ordered structure.

Introduction

It is very important to develop a new controlled polymerization method and concept for the synthesis of condensation polymers, which brings new materials with excellent properties, such as high thermal stability, strength, and electrical conductivity.

Most condensation polymers are prepared by the reaction between two different bifunctional symmetric monomers (XaaX and YbbY), yielding the −aabb− repeating units. The synthesis of ordered condensation polymers from nonsymmetric monomers, however, has been little explored. The ordered polymers are expected to show excellent thermal, mechanical, and optical properties compared to the random polymers. Therefore, we have been interested in the development of synthetic method for the ordered polymers from nonsymmetric monomers by direct polycondensation. In the previous studies, the new methods for the synthesis of ordered polymers from a symmetric monomer and a nonsymmetric monomer,[1,2,3] or two nonsymmetric monomers[4,5,13] have been reported. Diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)-phosphonate (**1**, chemical structure shown in Scheme 1) has been used as a condensing agent, with which the carboxylic acids form active acyl intermediates such as carboxylic−phosphoric mixed anhydrides or active amides whose reactivity difference between each other is large enough to prepare the ordered polymer.

Our next target will be the synthesis of ordered polymer from three nonsymmetric monomers, XabX, YcdY, and ZefZ, by direct polycondensation. We found that the differentiation among the three amino or carboxyl groups, that is, the selective acylation was possible by using the active amides derived from carboxylic acids and condensing agent **1**.

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We now report a successful synthesis of ordered (−ccfebaddabef−) poly(amide−acylhydrazide−amide) by the direct polycondensation of two nonsymmetric monomers, 5-(3-carboxypropyl)-2-isopropoxybenzoic acid (XabX), and 4-aminobenzohydrazide (YefY), with a pair of symmetric monomers, bis(4-nitrophenyl) isophthalate (XccX) and piperazine (YddY), using condensing agent **1**. Here −ab− and −cc− represent the nonsymmetric and symmetric monomeric units in the chain, respectively, and X and Y are the leaving groups in the polymerization reaction. First, the model reactions were studied in detail to design the nonsymmetric monomers. Second, the designed monomers were synthesized. Finally, the preparation and characterization of the polymers were studied.

Experimental Section

Materials. *N*-Methyl-2-pyrrolidinone (NMP) was purified by vacuum distillation after stirring over powdered calcium hydride overnight, and then stored over 4 Å molecular sieves. Piperazine (**10**) was purified by recrystallization from ethanol. 4-Aminobenzohydrazide (**11**) was prepared from methyl-4-aminobenzoate and hydrazine monohydrate according to the reported procedure.[9] Bis(4-nitrophenyl) isophthalate (**9**) was prepared by the condensation of 4-nitrophenol and isophthaloyl dichloride according to the reported procedure.[4] Triethylamine (TEA) and tetrahydrofuran (THF) were purified by the usual method. Other reagents and solvents were obtained commercially and used as received.

The condensing agent diphenyl (2,3-dihydro-2-thioxo-3-benzoxazolyl)phosphonate (**1**) was prepared according to the reported procedure.[10]

***N*-(*o*-Ethoxybenzoyl)benzoxazoline-2-thione (3b).** The mixture of *o*-ethoxybenzoic acid (3.32 g, 20 mmol) and thionyl chloride ($SOCl_2$, 20 mL) was heated for 9 h at 75 °C with stirring. The excess $SOCl_2$ was removed by distillation. The residue was dissolved in THF (40 mL), to which a solution of 2-mercaptobenzoxazole (3.02 g, 20 mmol) and TEA (2.8 mL, 20 mmol) in THF (20 mL) was added dropwise at room

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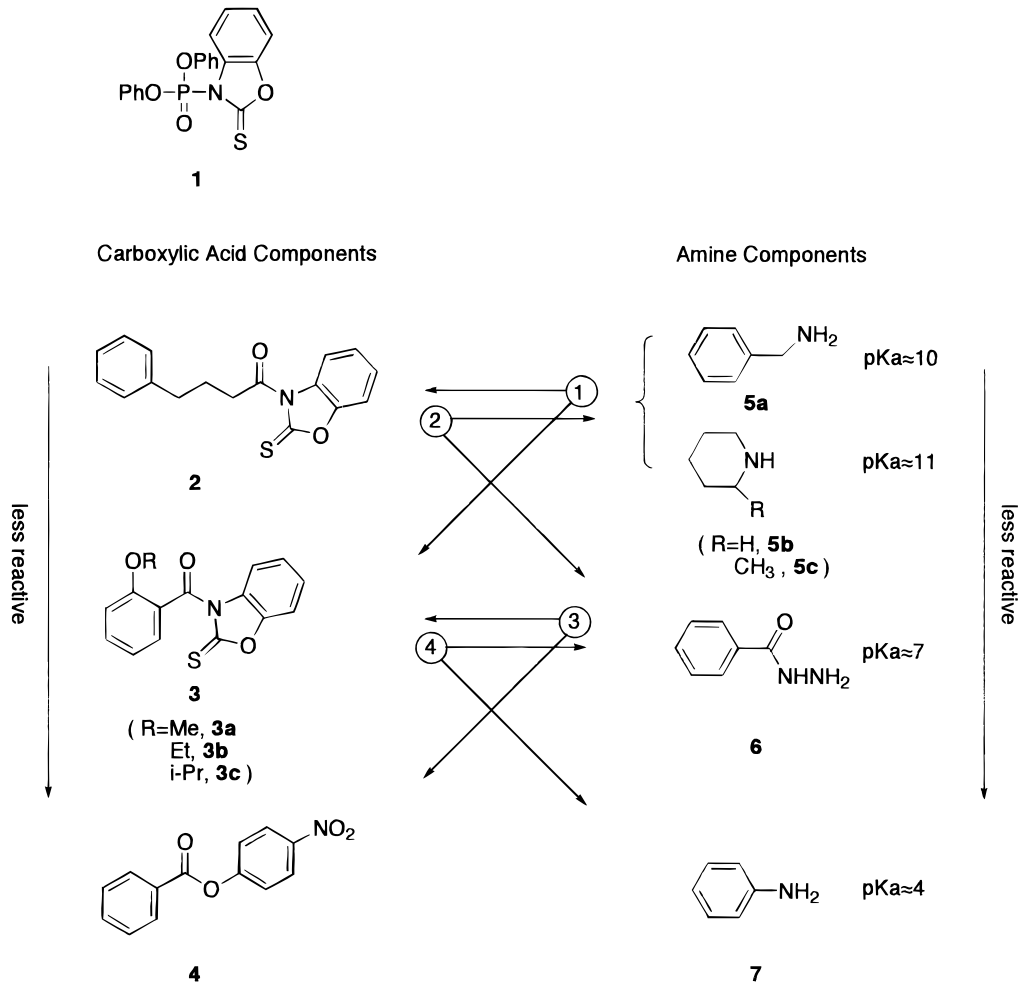
Scheme 1



temperature. After the reaction was stirred for 2 h, THF was evaporated and the residue was poured into 1% aqueous sodium hydrogen carbonate. The precipitate was recrystallized from ethanol to give yellow crystals, yield 4.27 g (71%). Mp: 131.5−133.5 °C. IR (KBr, cm^{-1}): 1697 (C═O). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 6.85−7.73 (m, 8H), 3.73−3.98 (q, J = 6.8 Hz, 2H), 1.00−1.06 (t, J = 6.8 Hz, 3H). Anal. Calcd: C, 64.20; H, 4.38; N, 4.68. Found: C, 64.48; H, 4.31; N, 4.62.

***N*-(4-Phenylbutanoyl)benzoxazoline-2-thione (2).** Compound **2** was synthesized by the same method described above to give white needles, yield 82%. Mp: 81.5−82.5 °C. IR (KBr, cm^{-1}): 1720 (C═O). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 8.06−8.10 (m, 1H), 7.17−7.37 (m, 8H), 3.52−3.57 (t, J = 7.2 Hz, 2H), 2.75−2.81 (t, J = 7.3 Hz, 2H), 2.10−2.21 (quint, J = 7.5 Hz, 2H). Anal. Calcd: C, 68.66; H, 5.08; N, 4.71. Found: C, 68.64; H, 5.05; N, 4.63.

***N*-(*o*-Methoxybenzoyl)benzoxazoline-2-thione (3a).** Compound **3a** was synthesized by the same method described above to give yellow crystals, yield 89%. Mp: 140−141 °C. IR (KBr, cm^{-1}): 1695 (C═O). Anal. Calcd: C, 63.15; H, 3.89; N, 4.91. Found: C, 63.26; H, 3.98; N, 4.93.

***N*-(*o*-Isopropoxybenzoyl)benzoxazoline-2-thione (3c).** A mixture of methyl salicylate (10.3 mL, 80 mmol), isopropyl bromide (9.3 mL, 99 mmol), anhydrous potassium carbonate (13.4 g, 97 mmol), sodium iodide (0.6 g, 4.0 mmol), and dry acetone (80 mL) was refluxed under nitrogen for 48 h.[7] At the end of this time the acetone was distilled from the mixture, 80 mL of water was added to the residue, and the product was extracted with two 40-mL portions of ether. The combined ether extracts were washed with three 40-mL portions of 5% aqueous sodium hydroxide, and the ether was removed by distillation. The residual oil was hydrolyzed over 10% aqueous sodium hydroxide at 80 °C for 30 min. After cooling, 70 mL of 2.4 M HCl was added for acidification. The product *o*-isopropoxybenzoic acid was then extracted with two 40-mL portions of ether and purified by column chromatography with ethyl acetate as the eluent, yield 6.0 g (42%). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 11.27 (s, 1H), 7.04−8.22 (m, 4H), 4.82−4.95 (sept, J = 5.9 Hz, 1H), 1.49−1.51 (d, J = 6.0 Hz, 6H).

Compound **3c** was synthesized by the same method as **3b** from *o*-isopropoxybenzoic acid to give light yellow crystals, yield 43%. Mp: 110.0−111.0 °C. IR (KBr, cm^{-1}): 1697 (C═O). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 6.83−7.67 (m, 8H), 4.11−4.54 (sept, J = 5.9 Hz, 1H), 1.03−1.05 (d, J = 5.9 Hz, 6H). Anal. Calcd: C, 65.16; H, 4.82; N, 4.47. Found: C, 65.09; H, 4.85; N, 4.41.

5-(3-Carboxypropyl)-2-isopropoxybenzoic Acid (8). Compound **8** was synthesized through four steps.

Methyl 5-(3-Carboxypropionyl)-2-hydroxybenzoate (8a). Into a mixture of succinic anhydride (5.0 g, 50 mmol), aluminum chloride (16.0 g, 120 mmol), and dichloromethane (50 mL) was added dropwise methyl salicylate (4.4 mL, 34 mmol) in dichloromethane (25 mL) at room temperature. After being stirred for 12 h, the reaction mixture was poured into distilled water (1 L) and extracted by ethyl acetate. After evaporation of the solvent, 10% aqueous sodium hydrogen carbonate (80 mL) and then *n*-hexane (30 mL) were added. The aqueous layer was acidified with 2 M HCl. The precipitate was filtered, dried, and recrystallized from ethanol to give yellow needles, yield 4.15 g (52%). Mp: 145.0−146.0 °C. IR (KBr, cm^{-1}): 1670, 2400−3400 (C═O, COOH); 1700 (C═O, ketone). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 11.26 (s, 1H), 8.52−8.53 (d, J = 1.9 Hz, 1H), 8.09−8.13 (dd, J = 1.9, 8.9 Hz, 1H), 7.04−7.07 (d, J = 8.9 Hz, 1H), 4.00 (s, 3H), 3.26−3.30 (t, J = 6.5 Hz, 2H) 2.80−2.84 (t, J = 6.5 Hz, 2H). Anal. Calcd: C, 57.14; H, 4.80. Found: C, 57.16; H, 4.78.

Methyl 5-(3-Methoxycarbonylpropionyl)-2-hydroxybenzoate (8b). Compound **8a** (4.15 g, 16.5 mmol) was dissolved in methanol (50 mL), and concentrated H_2SO_4 (1.5 mL) was added to the mixture. The resulting solution was refluxed for 5 h and then allowed to cool to room temperature. After methanol was removed, the residue was washed with 5% aqueous sodium hydrogen carbonate (50 mL) and extracted by ethyl acetate. The organic layer was separated, and the solvent was evaporated. Recrystallization from methanol gave light yellow needles, yield 3.94 g (90%). Mp: 112.5−114.0 °C. IR (KBr, cm^{-1}): 1720, 1674 (C═O). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 11.25 (s, 1H), 8,53−8.54 (d, J = 2.0 Hz, 1H), 8.10−8.14 (dd, J = 2.1, 8.9 Hz, 1H), 7.03−7.07 (d, J = 8.9 Hz, 1H), 4.00 (s, 3H), 3.72 (s, 3H), 3.26−3.31(t, J = 6.5 Hz, 2H) 2.75−2.80 (t, J = 6.5 Hz, 2H).

5-(3-Carboxypropionyl)-2-isopropoxybenzoic Acid (8c).[7] A mixture of **8b** (3.94 g, 14.8 mmol), isopropyl bromide (3.0 mL, 32.0 mmol), anhydrous potassium carbonate (4.14 g, 30.0 mmol), sodium iodide (0.1 g, 0.7 mmol), 18-crown-6 (52 mg, 0.2 mmol), and distilled NMP (40 mL) was heated to 100 °C for 12 h. After cooling, 100 mL of water and 100 mL of ether were added. The organic layer was washed with two 30-mL portions of 5% aqueous sodium hydroxide. The ether was removed by distillation. The residual oil was hydrolyzed over 10% aqueous sodium hydroxide at 90 °C for 3 h. After cooling, 2 M HCl was added for acidification. The precipitate was recrystallized from ethyl acetate to give light yellow crystals, yield 2.37 g (57%). Mp: 154.0−155.5 °C. IR (KBr, cm^{-1}): 1705 (C═O), 2400−3400 (COOH).^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 12.49 (broad, 2H), 8.18−8.19 (d, J = 2.2 Hz, 1H), 8.06−8.10 (dd, J = 2.3, 8.9 Hz, 1H), 7.24−7.28 (d, J = 9.0 Hz, 1H), 4.77−4.86 (sept, J = 5.9 Hz, 1H), 3.18−3.23 (t, J = 6.0 Hz, 2H), 2.54−2.59 (t, J = 6.1 Hz, 2H), 1.30−1.32 (d, J = 6.0 Hz, 6H).

5-(3-Carboxypropyl)-2-isopropoxybenzoic Acid (8).[8] Compound **8c** (2.37 g, 8.4 mmol), potassium hydroxide (1.55 g, 27.7 mmol), and 85% hydrazine monohydrate (1.76 mL, 30.0 mmol) were dissolved in diethylene glycol (9 mL) while heating. After the reaction was kept under reflux for 1.5 h, the water was drained from the condenser and the temperature allowed to rise to 180 °C, at which temperature the reaction was kept for 6 h. The cooled solution was diluted with 12 mL of water and poured slowly into 10 mL of 6 M HCl. The product was extracted by ethyl acetate. After the solvent was removed, the light yellow product was obtained through column chromatography (eluent: ethyl acetate/acetone/acetic acid (90/15/1)), yield 2.05 g (91%). Mp: 79.0−81.0 °C. IR (KBr, cm^{-1}): 1689 (C═O), 2400−3400 (COOH). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 12.24 (broad, 2H), 7.41−7.42 (d, J = 1.9 Hz, 1H), 7.25−7.29 (dd, J = 1.9, 8.9 Hz, 1H), 7.03−7.06 (d, J = 8.9 Hz, 1H), 4.52−4.65 (sept, J = 5.9 Hz, 1H), 2.52−2.57 (t, J = 7.6 Hz, 2H), 2.18−2.23 (t, J = 7.3 Hz, 2H), 1.70−1.81 (quint, J = 7.3 Hz, 2H), 1.24−1.28 (d, J = 5.7 Hz, 6H). Anal. Calcd: C, 63.15; H, 6.81. Found: C, 63.23; H, 6.93.

Competitive Reaction of 2 and 3c with Benzylamine (5a). Compound **5a** (0.11 mL, 1 mmol) was added to a solution of **2** (0.297 g, 1 mmol), **3c** (0.313 g, 1 mmol) and acetanilide (0.135 g, 1 mmol) in NMP (2.5 mL) at −15 °C and room temperature, respectively. The solution was stirred for 1 h. Then the ratio of the two products was determined by HPLC according to the calibration curves of each product with acetanilide as a standard substance.

Other Competitive Reactions. Other competitive reactions were carried out in the similar ways as described above.

Model Compounds. 1-{5-[4-(1-Piperidyl)-4-oxobutyl](2-isopropoxybenzoyl)}piperidine (12). Condensing agent **1** (0.422 g, 1.1 mmol) was added to a solution of **8** (0.133 g, 0.5 mmol), piperidine (0.10 mL, 1 mmol), and TEA (0.14 mL, 1 mmol) in NMP (2 mL) at room temperature. The solution was stirred for 3 h and poured into 10% aqueous sodium hydrogen carbonate. The product was extracted by ethyl acetate. After the solvent was removed, the product was obtained through column chromatography with ethyl acetate as the eluent, yield 0.181 g(90%). Mp: 80−82 °C. IR (KBr, cm^{-1}): 1628 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 7.78−7.13 (m, 3H), 4.45−4.54 (sept, J = 6.1 Hz, 1H), 3.10−3.79 (m, 8H), 2.56−2.63 (t, J = 7.4 Hz, 2H), 2.29−2.35 (t, J = 7.4 Hz, 2H), 1.87−1.98 (quint, J = 7.9 Hz, 2H), 1.54−1.63 (m, 12H), 1.29−1.30 (d, J = 6.2 Hz, 6H). ^{13}C NMR (DMSO-d_6): 170.4, 167.0 (C═O), 151.6, 134.3, 129.9, 127.8, 127.7, 114.1 (aromatic), 70.1, 24.3 (isopropyl), 47.4, 46.0, 42.0, 26.3, 25.5, 22.0 (piperidine), 33.8, 31.8, 27.0 (propylene).

***N′*-Benzoyl-5-[4-(*N′*-benzohydrazino)-4-oxobutyl]-2-isopropoxybenzohydrazide (13)**. This model compound was prepared from **8** and benzohydrazide as described above. The yield was 92%. Mp: 97−99 °C. IR (KBr, cm^{-1}): 1689, 1651, 1628 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 10.95 (s, 1H), 10.34 (s, 1H), 10.23 (s, 1H), 9.91 (s, 1H), 7.17−7.97 (m, 13H), 4.79−4.82 (sept, J = 6.4 Hz, 1H), 2.62−2.68 (t, J = 7.0 Hz, 2H), 2.22−2.27 (t, J = 6.8 Hz, 2H), 1.85−1.90 (quint, J = 6.8 Hz, 2H), 1.37−1.40 (d, J = 6.2 Hz, 6H). ^{13}C NMR (DMSO-d_6): 171.7, 165.8, 165.0, 164.2 (C═O), 153.9, 134.2, 133.0, 132.6, 132.3, 132.0, 130.5, 128.6, 127.7, 127.6, 124.9, 123.4, 122.0, 115.2 (aromatic), 71.8, 21.7 (isopropyl), 33.4, 32.7, 27.0 (propylene).

5-(3-*N′*-Phenylcarbamoylpropyl)-2-isopropoxybenzanilide (14). This model compound was prepared from **8** and aniline as described above. The yield was 91%. Mp: 145−146 °C. IR (KBr, cm^{-1}): 1658 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 10.18 (s, 1H), 9.91 (s, 1H), 7.03−7.74 (m, 13H), 4.72−4.75 (sept, J = 5.9 Hz, 1H), 2.61−2.66 (t, J = 6.9 Hz, 2H), 2.33−2.37 (t, J = 6.4 Hz, 2H), 1.88−1.92 (quint, J = 7.0 Hz, 2H), 1.36−1.38 (d, J = 5.8 Hz, 6H). ^{13}C NMR (DMSO-d_6): 171.2, 164.2 (C═O), 153.5, 139.5, 139.1, 134.1, 132.4, 130.3, 129.1, 128.7, 124.5, 123.7, 123.1, 119.6, 119.2, 115.0 (aromatic), 71.7, 21.8 (isopropyl), 35.7, 33.6, 26.8 (propylene).

***N*,*N′*-Isophthaloyldipiperidine (15).** This compound was prepared from isophthaloyl dichloride and piperidine in the presence of TEA in THF. Recrystallization from methanol gave white crystals, yield 80%. Mp: 72−75 °C. IR (KBr, cm^{-1}): 1628 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 7.32−7.51 (m, 4H), 3.27−3.58 (m, 8H), 1.49−1.60 (m, 12H). ^{13}C NMR (DMSO-d_6): 168.4 (C═O), 136.8, 128.9, 127.6, 124.7 (aromatic), 48.0, 42.3, 25.8 (piperidine).

***N′*,*N′*-Benzoylisophthalodihydrazide (16).** Recrystallization from acetic acid gave white crystals, yield 87%. Mp: 290−291 °C. IR (KBr, cm^{-1}): 1643, 1682 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 10.72 (s, 2H), 10.62 (s, 2H), 7.52−8.52 (m, 14H). ^{13}C NMR (DMSO-d_6): 166.0, 165.4 (C═O), 133.2, 132.6, 132.1, 130.7, 129.0, 128.7, 127.6, 127.2 (aromatic).

Isophthalanilide (17). Recrystallization from acetic acid gave white crystals, yield 95%. Mp: 291−293 °C. IR (KBr, cm^{-1}): 1643 (C═O). ^{1}H NMR (δ, ppm, TMS, DMSO-d_6): 10.46 (s, 2H), 7.11−8.19 (m, 14H). ^{13}C NMR (DMSO-d_6): 165.3 (C═O), 139.2, 135.4, 130.8, 128.8, 128.7, 127.2, 124.0, 120.5 (aromatic).

Authentic Ordered Poly(amide−acylhydrazide−amide) (20). *N*,*N′*-{5,5′-[3,3′-(piperazine-1,4-dicarbonyl)dipropylene]bis(2-isopropoxybenzoyl)}bis(benzoxazoline-2-thione) (18). Condensing agent **1** (0.843 g, 2.2 mol) was added to a solution of **8** (0.266 g, 1.0 mmol) and TEA (0.28 mL, 2.0 mmol) in NMP (4 mL). The solution was stirred for 3 h, to which **10** (0.043 g, 0.5 mmol) was added at −15 °C. The resulting solution was stirred for 1 h and poured into 5% aqueous sodium carbonate. The light yellow precipitate was filtered out and dried, yield 0.323 g (76%). Mp: 172−175 °C. IR (KBr, cm^{-1}): 1705, 1651 (C═O). ^{1}H NMR (δ, ppm, TMS, $CDCl_3$): 7.65−7.77 (m, 14H), 4.40−4.48 (sept, J = 5.9 Hz, 2H), 3.40−3.62 (m, 8H), 2.68−2.73 (t, J = 7.3 Hz, 4H), 2.30−2.36 (t, J = 6.8 Hz, 4H), 1.98−2.02 (quint, J = 5.9 Hz, 4H), 1.00−1.04 (d, J = 6.2 Hz, 12H). Anal. Calcd for $C_{46}H_{48}N_4O_8S_2\cdot 0.4H_2O$: C, 64.53; H, 5.74; N, 6.54. Found: C, 64.59; H, 5.79; N, 6.40.

5,5′-[3,3′-(Piperazine-1,4-dicarbonyl)dipropylene]bis-[N′-(4-aminobenzoyl)-2-isopropoxybenzohydrazide] (19). 4-Aminobenzohydrazide (**11**) (0.091 g, 0.6 mmol) was added to the solution of compound **18** (0.255 g, 0.3 mmol) in NMP (2 mL) at room temperature. After being stirred for 24 h, the reaction mixture was poured into 5% aqueous sodium carbonate. The precipitate **19** was filtered out, dried, and recrystal-

lized from methanol, yield 0.204 g (80%). Mp: 148−150 °C. IR (KBr, cm^{-1}): 1628 (C═O). ^1H NMR (δ, ppm, TMS, DMSO-d_6): 10.40−10.41 (d, J = 1.9 Hz, 2H), 10.11−10.12 (d, J = 1.8 Hz, 2H), 6.55−7.68 (m, 14H), 5.75 (s, 4H), 4.77−4.81 (sept, J = 6.2 Hz, 2H), 3.24−3.45 (m, 8H), 2.58−2.61 (t, J = 7.4 Hz, 4H), 2.32−2.37 (t, J = 6.8 Hz, 4H), 1.76−1.83 (quint, J = 6.8 Hz, 4H), 1.34−1.37 (d, J = 5.9 Hz, 12H). ^{13}C NMR (DMSO-d_6): 170.8, 164.9, 163.8 (C═O). Anal. Calcd for $C_{46}H_{56}N_8O_8 \cdot 2.1H_2O$: C, 62.19; H, 6.83; N, 12.61. Found: C, 62.14; H, 6.97; N, 12.50.

Compound **19** (0.170 g, 0.2 mmol) was dissolved in NMP (0.4 mL) at room temperature. The solution was cooled in a dry ice−acetone bath, to which isophthaloyl dichloride (0.041 g, 0.2 mmol) was added in one portion, and the cooling bath was changed to ice−water. The mixture was stirred for 1 h at 0 °C and then 1 h at room temperature. The resulting polymer solution was diluted with NMP (0.4 mL) and precipitated by pouring the solution into methanol. The precipitate was filtered out, washed with methanol and dried, yield 0.137 g (70%). The inherent viscosity of polymer in NMP was 0.48 dL/g, measured at a concentration of 0.5 g/dL at 30 °C. IR (KBr, cm^{-1}): 1620−1660, 1527 (C═O). ^1H NMR (δ, ppm, TMS, DMSO-d_6): 10.89 (s, 2H), 10.72 (s, 2H), 10.22 (s, 2H), 8.55 (s, 1H), 8.19−8.21 (d, 2H), 7.98 (s, 8H), 7.72−7.76 (t, 1H), 7.67 (s, 2H), 7.33−7.37 (d, 2H), 7.13−7.17 (d, 2H), 4.75−4.78 (m, 2H), 3.42−3.44 (m, 8H), 2.57−2.61 (t, 4H), 2.32−2.37 (t, 4H), 1.77−1.81 (m, 4H), 1.36−1.38 (d, 12H). ^{13}C NMR (DMSO-d_6): 170.8, 165.6, 164.3, 164.0 (C═O). Anal. Calcd for $C_{54}H_{58}N_8O_{10} \cdot 1.8H_2O$: C, 64.12; H, 6.14; N, 11.08. Found: C, 64.15; H, 6.28; N, 10.92.

Poly(amide−acylhydrazide−amide) Prepared by Direct Polycondensation (21). Condensing agent **1** (0.843 g, 2.2 mmol) was added to a solution of **8** (0.266 g, 1.0 mmol), **9** (0.263 g, 0.5 mmol), and TEA (0.28 mL, 2.0 mmol) in NMP (2 mL). The solution was stirred at room temperature for 3 h and cooled to −15 °C. To the resulting solution was added a solution of **10** (0.043 g, 0.5 mmol) and **11** (0.151 g, 1.0 mmol) in NMP (1 mL). Then the solution was stirred at −15 °C for 2 h and room temperature for 24 h. 1-Hydroxybenzotriazole (HOBt) (0.015 g, 0.1 mmol) was added before the solution was heated to 70 °C. The solution was kept at 70 °C for 4 d and poured into methanol. The precipitate was filtered out and dried, yield 0.445 g (91%). The inherent viscosity of polymer in NMP was 0.20 dL/g, measured at a concentration of 0.5 g/dL at 30 °C. IR (KBr, cm^{-1}): 1620−1660, 1527 (C═O). ^1H NMR (δ, ppm, TMS, DMSO-d_6): 10.89 (s, 2H), 10.72 (s, 2H), 10.22 (s, 2H), 8.55 (s, 1H), 8.19−8.21 (d, 2H), 7.98 (s, 8H), 7.72−7.76 (t, 1H), 7.67 (s, 2H), 7.33−7.37 (d, 2H), 7.13−7.17 (d, 2H), 4.79−4.81 (m, 2H), 3.42−3.44 (m, 8H), 2.57−2.61 (t, 4H), 2.32−2.37 (t, 4H), 1.77−1.81 (m, 4H), 1.37−1.39 (d, 12H). ^{13}C NMR (DMSO-d_6): 170.8, 165.6, 164.3, 164.0 (C═O). Anal. Calcd for $C_{54}H_{58}N_8O_{10} \cdot 2.8H_2O$: C, 63.00; H, 6.23; N, 10.88. Found: C, 63.11; H, 6.07; N, 10.60.

Random Poly(amide−acylhydrazide−amide) (22). Condensing agent **1** (0.843 g, 2.2 mmol) was added to a solution of **8** (0.266 g, 1.0 mmol), **9** (0.263 g, 0.5 mmol), **10** (0.043 g, 0.5 mmol), **11** (0.151 g, 1.0 mmol), and TEA (0.28 mL, 2.0 mmol) in NMP (2 mL). The mixture was stirred at room temperature for 3 h and 80 °C for 12 h. The resulting solution was diluted with NMP (2 mL) and poured into methanol. The polymer was collected and dried, yield 0.362 g (74%). The inherent viscosity of polymer in NMP was 0.21 dL/g, measured at a concentration of 0.5 g/dL at 30 °C. IR (KBr, cm^{-1}): 1620−1660, 1527 (C═O). ^1H NMR (δ, ppm, TMS, DMSO-d_6): 9.94−11.02 (m, 6H), 7.01−8.60 (m, 18H), 4.50−4.90 (m, 2H), 3.20−3.90 (m, 8H), 1.80−2.801 (m, 12H), 0.87−1.37 (m, 12H). ^{13}C NMR (DMSO-d_6): 171.8, 170.9, 168.8, 167.3, 167.2, 167.1, 165.7, 165.4, 165.3, 164.9, 164.4, 164.0 (C═O). Anal. Calcd for $C_{54}H_{58}N_8O_{10} \cdot 2H_2O$: C, 63.89; H, 6.16; N, 11.04. Found: C, 64.24; H, 5.95; N, 10.51.

Measurements. The infrared spectra were recorded on a Horiba FT-210 IR spectrophotometer and the NMR spectra on a JEOL EX 270 (270 MHz) spectrometer. Viscosity measurements were carried out with an Ostwald viscometer at 30 °C. Thermal analyses were performed on a Seiko SSS 5000 TG/DTA 220 thermal analyzer at a heating rate of 10 °C/min for thermogravimetric analysis.

Results and Discussion

When we use two nonsymmetric monomers XabX and YefY, and a pair of symmetric monomers, XccX and YddY, as a nonsymmetric monomer, the elementary reactions of these monomers would yield the following structure elements in the polymer chain, −ad−, −ae−, −af−, −bd−, −be−, −bf−, −cd−, −ce−, and −cf−. Let us assume X as a carboxylic acid group or its derivative and the reactivities of aX, bX, and cX increase in the order cX < bX < aX, while with Y as the amine group, the reactivities of dY, eY, and fY increase in the order fY < eY < dY. When the rate constant k_{ad} is much larger than all the others, such as k_{ae} and k_{bd}, the first intermediate will be XbaddabX; Then when k_{be} is much larger than k_{bf} and k_{ce}, the second intermediate will be YfebaddabefY, which will later polymerize stoichiometrically with XccX to give the fully ordered (−ccfebaddabef−) polymer.

The choice of monomers is the most important in the preparation of the ordered polymers from three nonsymmetric monomers by direct polycondensation using condensing agent **1**, and the electrophilicity and nucleophilicity of each monomer should be controlled carefully. For this, three types of electrophiles, carboxylic acid components, and three types of nucleophiles, amine components, were determined.

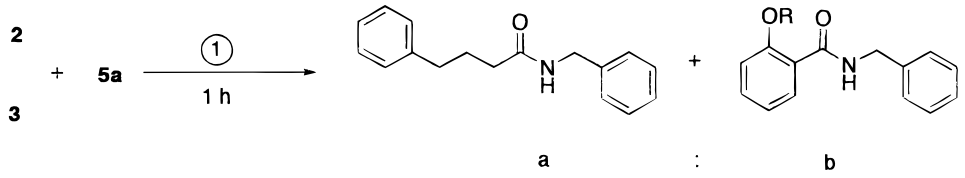
Selection of the Carboxylic Components. Aromatic acid derivatives are generally less reactive toward nucleophiles than aliphatic acid derivatives due to the delocalization of the positive charge on the carbonyl carbon into the aromatic ring. At the same time, the steric effect, e.g., due to *o*-substituted aromatic carboxylic acid, helps to enlarge the reactivity difference. We have reported the competitive reaction between lauric acid and *o*-toluic acid in the presence of **1**, with benzohydrazide, where the active intermediates are active amides.[5] Selective amidation was observed, and *N′*-benzoyllaurohydrazide was obtained in quantitative yield. The third carboxylic acid derivative should be much less reactive than the active amides. In a previous paper,[11] we reported polyamide synthesis by 1-hydroxybenzotriazole- (HOBt) catalyzed polycondensation of active aromatic diesters with aromatic diamines, where bis(4-nitrophenyl) isophthalate reacted slowly with aromatic diamines at 70 °C, but gave a high molecular weight of polyamide. The competitive reaction between *o*-anisic acid and 2,4,6-trichlorophenylbenzoate with amines, such as phenethylamine, benzohydrazide, and aniline, in the presence of **1** was also reported, and in all cases, selective amidation was observed.[4]

On the basis of these findings, aliphatic carboxylic acid, *o*-substituted aromatic carboxylic acid, and active ester seemed to be good candidates for three types of electrophiles; e.g., 4-phenylbutyric acid, *o*-alkoxybenzoic acid, and 4-nitrophenyl benzoate were selected as three carboxylic acid components.

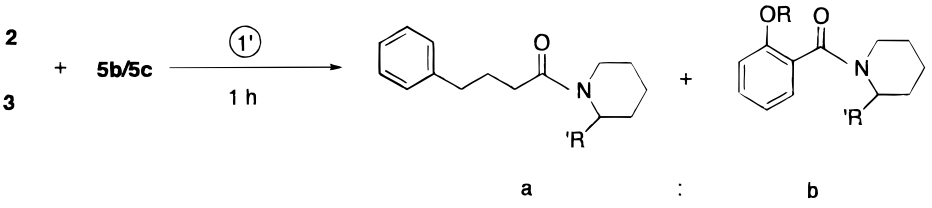
Selection of the Amine Components. The linear relationship between log k (second-order constant) and pK_a of aniline derivatives for the reaction of benzoic acid with various anilines in NMP in the presence of **1** has been reported.[6] Therefore, a similar relationship would be expected for the reaction of active amides with amines.

The competitive reactions between 2-phenethylamine (pK_a = 10) or benzohydrazide (pK_a = 7) and aniline (pK_a

Scheme 2

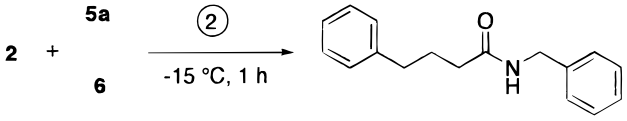


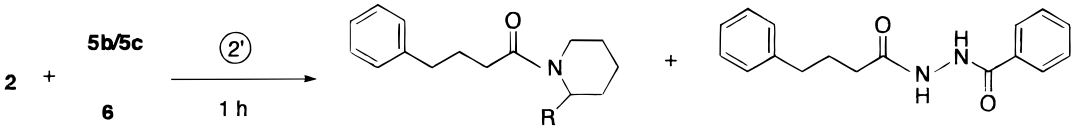
temp. (°C)	R = Me	Et	i-Pr
20	73 : 29	82 : 18	86 : 14
-15	79 : 21	85 : 15	91 : 9



	temp. (°C)	R = Me	Et	i-Pr
R' = H	20	85 : 15	88 : 12	93 : 7
	-15	93 : 7	94 : 6	100: 0
R' = CH_3	20	93 : 7	100 : 0	
	-15	95 : 5	100 : 0	

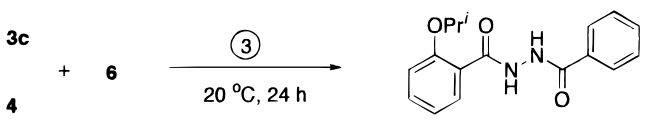
Scheme 3





- 20 °C		
R = H	99	1
R = CH_3	49	51

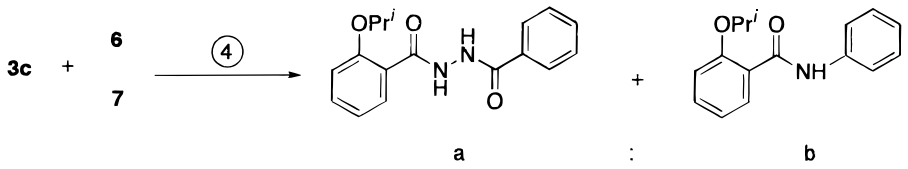
Scheme 4



= 4) with benzoic acid were studied in the presence of **1** and gave the product *N*-phenethylbenzamide or *N′*-benzoylbenzohydrazide, respectively, in quantitative yield.[4] Therefore, aliphatic amine, acylhydrazide, and aromatic amine are chosen as three types of nucleophiles, such as benzylamine (**5a**, pK_a = 10)/piperidine (**5b**, pK_a = 11)/2-pipecoline (**5c**, pK_a = 11), benzohydrazide (**6**), and aniline (**7**).

Competitive Reactions and Design of Nonsymmetric Monomers. With **1** as a condensing agent, the carboxylic acids can form active amides to enlarge the reactivity difference between each other. Therefore, the compounds in Scheme 1 were selected for the model reactions to investigate the reactivities. The arrows labeled with numbers 1 to 4 indicate the combination of each competitive reaction.

Scheme 5



temp.(°C) / time (h)		
20 / 24	94	6
-20 / 48, 0 / 24, 20 / 24	96	4

To demonstrate the possibility of the formation of ordered polymer, the four competitive reactions noted in Scheme 1 have been carried out.

First, the competitive reaction of the active amides *N*-(4-phenylbutanoyl)benzoxazoline-2-thione (**2**) and *N*-(*o*-methoxybenzoyl)benzoxazoline-2-thione (**3a**)/*N*-(*o*-ethoxybenzoyl)benzoxazoline-2-thione (**3b**)/*N*-(*o*-isopropoxybenzoyl) benzoxazoline-2-thione (**3c**) toward benzylamine (**5a**)/piperidine (**5b**)/2-pipecoline (**5c**) was performed to determine whether the selective amidation would occur or not. The molar ratios of products a and b obtained are shown in Scheme 2. It is obvious that the selectivity increases when the alkoxy group becomes larger due to the larger steric hindrance. When benzylamine was used as a nucleophile, the best ratio of two products was 91:9 at −15 °C. The high nucleophilicity of benzylamine should be partially responsible for its poor selectivity when it reacts with active amides. Therefore, secondary amines such as **5b** and **5c** were used instead of benzylamine, and selective amidations were observed in the cases of **2** and **3c** toward **5b** and **2** and **3b** toward **5c**, respectively.

Second, the competitive reaction of **2** with **5a** and benzohydrazide (**6**) was carried out at −15 °C in NMP (Scheme 3), and formed the desired product *N*-benzyl-4-phenylbutyric amide quantitatively. When **5b** or **5c** was used instead of **5a**, **5b** exhibited much higher reactivity than **5c**, with the ratio of two products being up to 99:1. So piperazine (**10**) was selected to be one of the diamine monomers and 5-(3-carboxypropyl)-2-isopropoxybenzoic acid (**8**) to be a nonsymmetric dicarboxylic acid.

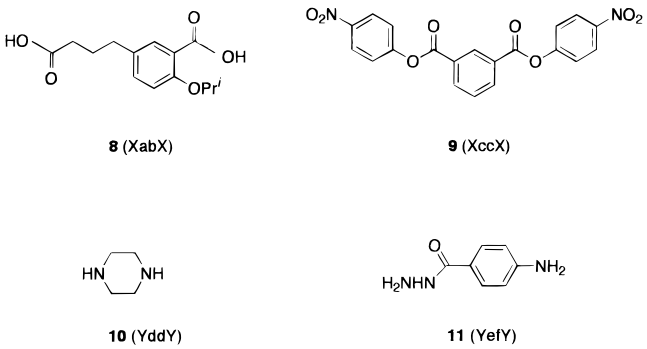
Next, the selective aminolysis of **3c** and 4-nitrophenyl benzoate (**4**) toward **6** was studied. Compound **6** reacted with **3c** selectively, yielding *N*′-benzoyl(2-isopropoxy)-benzohydrazide quantitatively (Scheme 4).

Finally, the competitive reaction of **6** and aniline (**7**) with **3c** was carried out, and 96% of desired product, *N*′-benzoyl(2-isopropoxy)benzohydrazide was obtained (Scheme 5). Although the reactivity of **3c** is so low that it takes a much longer time to complete the reactions, the selectivity is acceptable. Moreover, when 4-aminobenzohydrazide as the nonsymmetric diamine is selected, the reactivity difference between acylhydrazide and aromatic amine will be enlarged due to their electronic effects and thus the selectivity is expected to increase.

On the basis of these model reactions and the availability of the chemical reagents, 5-(3-carboxypropyl)-2-isopropoxybenzoic acid (**8**, XabX), bis(4-nitrophenyl) isophthalate (**9**, XccX), piperazine (**10**, YddY) and 4-aminobenzohydrazide (**11**, YefY), as shown in Scheme 6, were chosen as three nonsymmetric monomers, which were hopefully to give an sequential structure by direct polycondensation.

To clarify the structure of the polymers obtained, the model compounds in Scheme 7 were prepared from the corresponding carboxylic acids and amines in the presence of **1**, or isophthaloyl dichloride and corresponding amines. The data in the scheme show the chemical

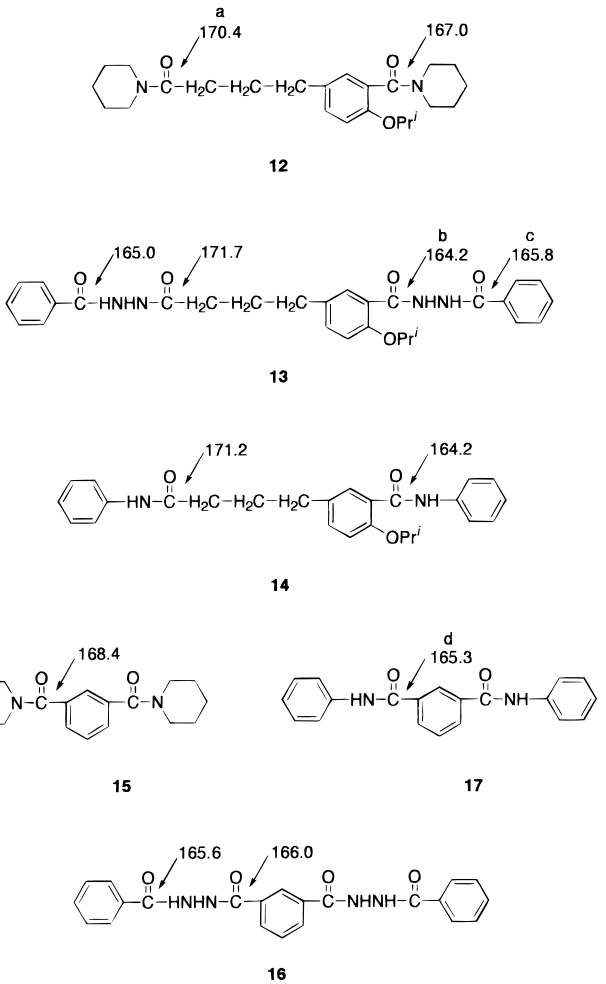
Scheme 6



8 (XabX) **9** (XccX)

10 (YddY) **11** (YefY)

Scheme 7



12

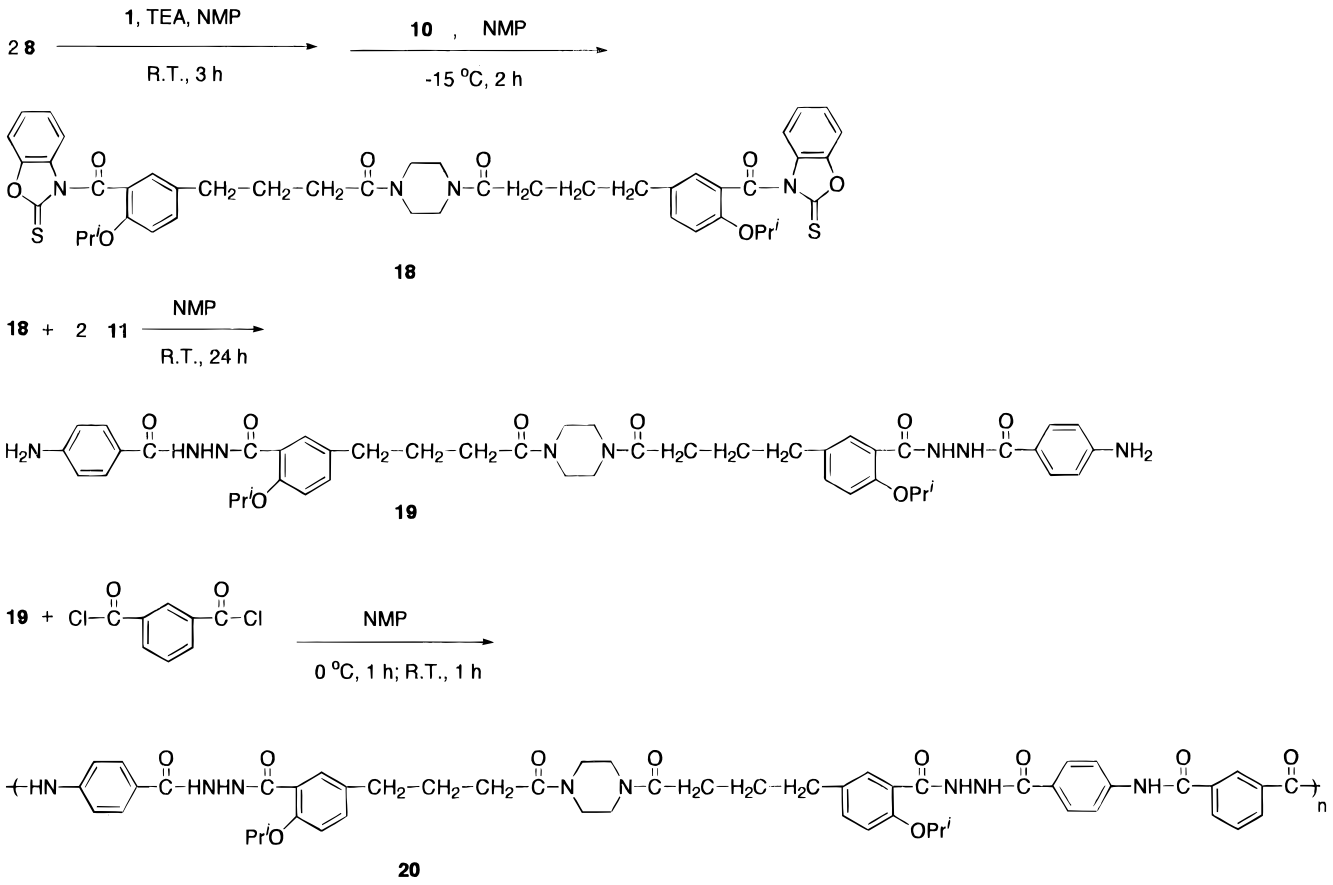
13

14

15 **17**

16

Scheme 8



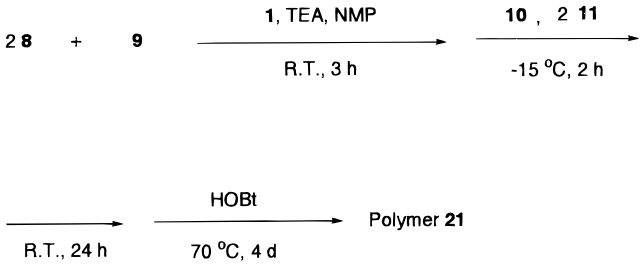
shifts of carbonyl groups in ^{13}C NMR spectra. All of the peaks are possible to appear in the random polymer, but only peaks a, b, c, and d are expected to appear in the ordered polymer.

Polymer Synthesis. Synthesis of Authentic Ordered Poly(amide−acylhydrazide−amide) (20). The authentic ordered polymer **20** was synthesized for the characterization of the structure of ordered polymer obtained by direct polycondensation. Authentic polymer **20** was prepared as shown in Scheme 8.

The reaction of **8** with **10** in the presence of **1** yielded **18**, which was separated, purified, characterized, and then reacted with **11** to give **19**. The low-temperature solution polycondensation of isophthaloyl dichloride with **19** was carried out in NMP, giving poly(amide−acylhydrazide−amide) (**20**) with an inherent viscosity of 0.48 dL/g.

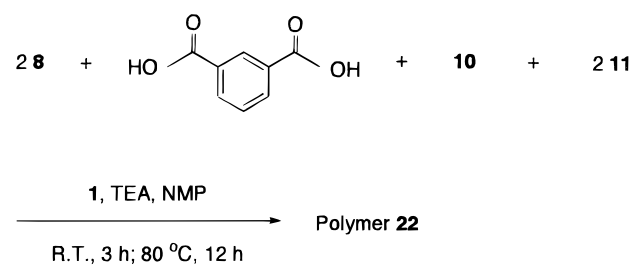
Synthesis of Ordered Poly(amide−acylhydrazide−amide) by Direct Polycondensation (21). The synthesis of the ordered polymer **21** was carried out by using a one-pot method. Condensing agent **1** was added to a solution of **8**, **9**, and TEA in NMP. The solution was stirred at room temperature for 3 h and cooled to −15 °C. To the resulting solution was added a solution of **10** and **11** in NMP. Then the solution was stirred at −15 °C for 2 h and room temperature for 24 h. 1-Hydroxybenzotriazole (HOBt) was added before the solution was heated to 70 °C, at which temperature the solution was kept for 4 d. The polycondensation procedure can be considered to involve the following three separate steps: (i) activation of the carboxylic acid component, i.e., generation of the active amide from **1** and carboxylic acid **8**, (ii) condensation of this intermediate with the amines, **10** at −15 °C for 2 h and **11** at room temperature for 24 h, respectively, and (iii) the polycondensation of the resulting amino−acylhydrazide−amide with active ester **9** in the presence of HOBt[11] as a catalyst. The polycondensation proceeded slowly and gave polymer **21** with an inherent viscosity of 0.20 dL/g (Scheme 9).

Scheme 9



Synthesis of Random Poly(amide−acylhydrazide−amide) (22). Random polymer with an inherent viscosity of 0.21 dL/g was synthesized from **8**, isophthalic acid, **10**, and **11** in the presence of **1** by mixing the four compounds at once (Scheme 10).

Scheme 10



Polymer Characterization. The IR spectra of the poly(amide−acylhydrazide−amide)s were identical and

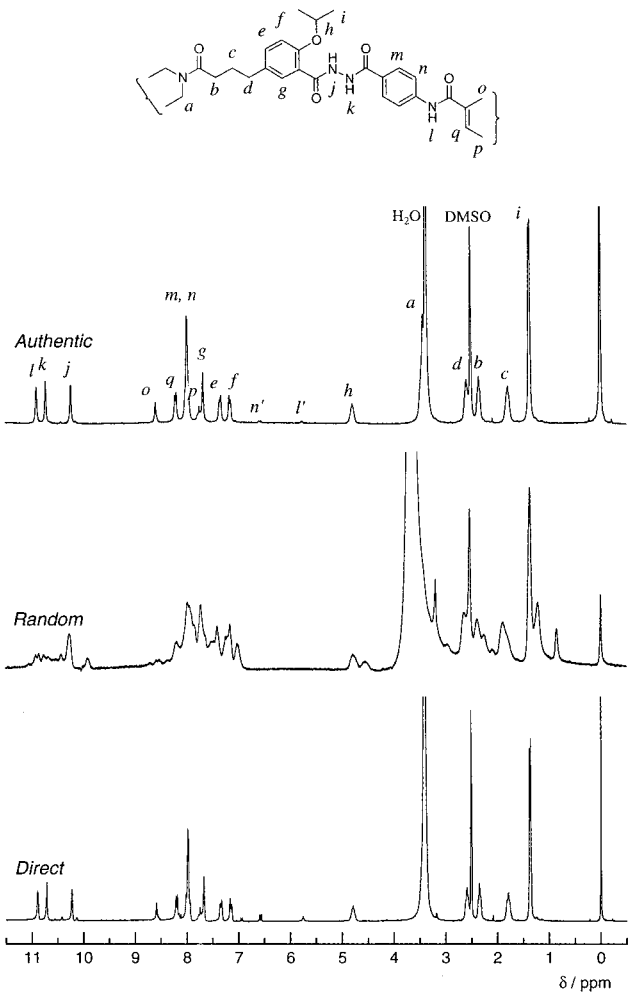


Figure 1. ^{1}H NMR spectra of polymers **20** (authentic), **21** (direct), and **22** (random) in DMSO-d_6 (n′, l′: see Scheme 11).

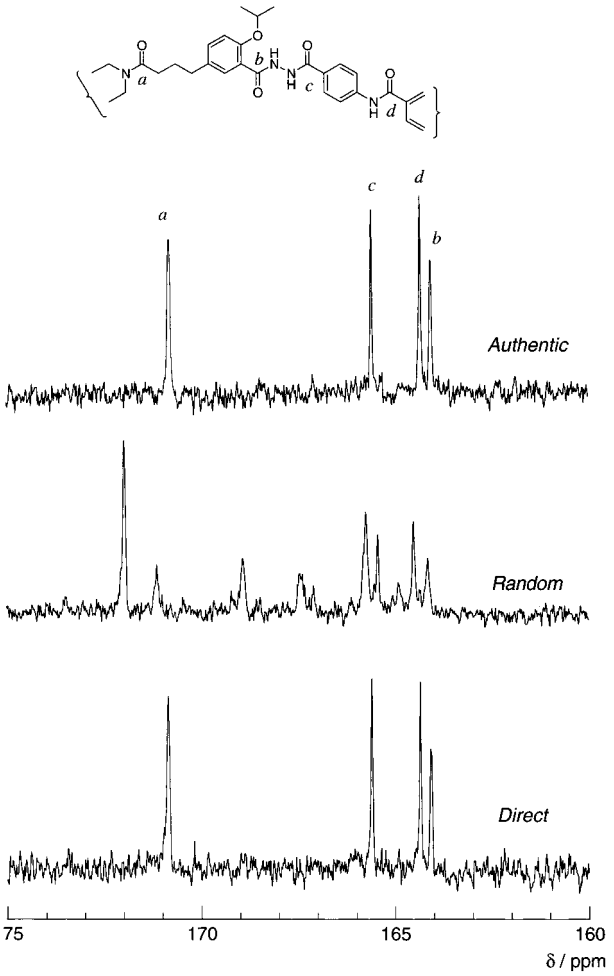
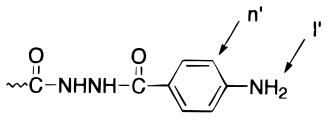


Figure 2. ^{13}C NMR spectra of polymers **20** (authentic), **21** (direct), and **22**(random) in DMSO-d_6.

consistent with those of model compounds and known analogues. All the polymers showed characteristic NH, amide I, and amide II bands in the ranges 3310, 1620−1640, and 1527 cm^{-1}, respectively. Elementary analysis also supported the formation of the expected polymers.

The microstructure of the polymers was determined by ^{1}H and ^{13}C NMR spectroscopy. Figure 1 shows the ^{1}H NMR spectra of authentic ordered polymer **20**, polymer **21** prepared by direct polycondensation, and random polymer **22**. It is clear that the spectra of polymers **20** and **21** are identical except for peak a, which was probably overlapped by the peak of H_2O in the solvent for polymer **21**, and the inset of Figure 1 shows the assignment of each resonance. Two small extra peaks for polymers **20** and **21** were observed at 5.75 and 6.55−6.58 ppm (peaks l′ and n′ in Figure 1), which would be derived from the end aminobenzoyl group as shown in Scheme 11. From the proton integral

Scheme 11



of the end amino group, the degree of polymerization is estimated to be 30 and 10 for authentic and direct polymers, respectively; i.e., the average molecular weight equals to 3.0×10^4 and 1.0×10^4, respectively. On the other hand, polymer **22** exhibits more peaks, indicating its random structure.

The ^{13}C NMR spectra of polymers **20**, **21**, and **22** are presented in Figure 2. The signals of carbon nuclei in amide carbonyl groups for polymers **20** and **21** appeared at 170.8, 165.6, 164.3, and 164.0 ppm. These peaks are assigned, as shown in the inset of Figure 2, on the basis of chemical shifts for model compounds. The 12 peaks of carbon nuclei in the amide carbonyl groups for the random polymer would be expected from its random structure. In fact, the 12 signals for random polymer **22** appeared at 171.8, 170.9, 168.8, 167.3, 167.2, 167.1, 165.7, 165.4, 165.3, 164.9, 164.4, and 164.0 ppm.

The above findings indicate that polymer **21** prepared by direct polycondensation was the desired ordered poly(amide−acylhydrazide−amide).

Polymer **20** is a white solid, while polymers **21** and **22** appear to be light brown. They are soluble in sulfuric acid and dipolar aprotic solvents such as NMP, DMF, DMSO, and pyridine and insoluble in other common organic solvents.

The thermal stability of the polymers was examined by thermogravimetry (TG) and differential thermal analysis (DTA). Typical traces for polymer **20** are shown in Figure 3. The weight loss starts from 295 °C in the TG trace, which is in good agreement with other polymers with an acylhydrazide component in the polymer chain,[4,5] ascribed to the weight loss of the elimination of water due to the 1,3,4-oxadiazole ring

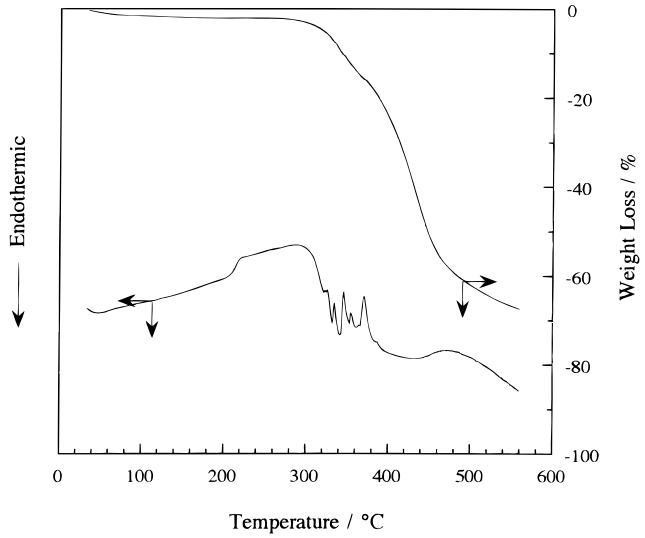


Figure 3. TG and DTA traces of polymer **20** in nitrogen.

formation. The second weight loss occurred immediately, which corresponds to the degradation of the polymer.

We expected differences in their properties owing to different regularities. However, no difference in the solubility and thermal stability among these poly(amide-acylhydrazide-amide)s can be detected. Pino et al. observed similar behavior in studies of the influence of constitutional isomerism on the physical properties of polycondensates and reported that unsubstituted polyamide might not be very suitable because strong effects brought about by extensive interchain NH−OC bonds might mask subtle effects due to isomerism.[12] Though we used secondary amine as one of the monomers, the strong intermolecular hydrogen bond from acylhydrazide and aromatic amide still masked the subtle effects caused by different regularity.

In summary, we have demonstrated that the synthesis of ordered poly(amide−acylhydrazide−amide) can be achieved by the direct polycondensation of a nonsymmetric carboxylic acid (**8**) and a symmetric active ester (**9**), with a nonsymmetric amine (**11**) and a symmetric amine (**10**), using condensing agent **1**.

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