

# Polymerization of 2,5-Diaminoterephthalic acid-Type Monomers for the Synthesis of Polyamides Containing Ladder Unit

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**ABSTRACT:** To synthesize ladder-type polyamides by construction of two amide bonds successively, 2,5-diaminoterephthalic acid derivatives bearing anthranilic acid ester and isatoic anhydride moieties were synthesized and their polymerization was investigated. Polymerization of the methyl ester monomer proceeded in the presence of lithium hexamethyldisilazide (LiHMDS) as a base in tetrahydrofuran (THF). However, mass spectroscopic analysis of the product suggested that not only the bis(trimethylsilyl)amide anion of LiHMDS but also the methoxide anion eliminated at the second amide-linkage formation reaction decomposed the isatoic anhydride unit of the growing

oligomer by nucleophilic attack to disturb the polymerization. To reduce the nucleophilicity of the eliminated anion, methyl ester of the monomer was changed to phenyl ester and its polymerization was studied. The reaction conditions were optimized, and the best result was obtained when the polymerization was conducted in the presence of 1.0 equivalent of LiHMDS without additives in THF at 50 °C. © 2017 Wiley Periodicals, Inc. *J. Polym. Sci., Part A: Polym. Chem.* **2017**, *00*, 000–000

**KEYWORDS:** anthranilic acid; isatoic anhydride; ladder; NMR; polyamides; synthesis

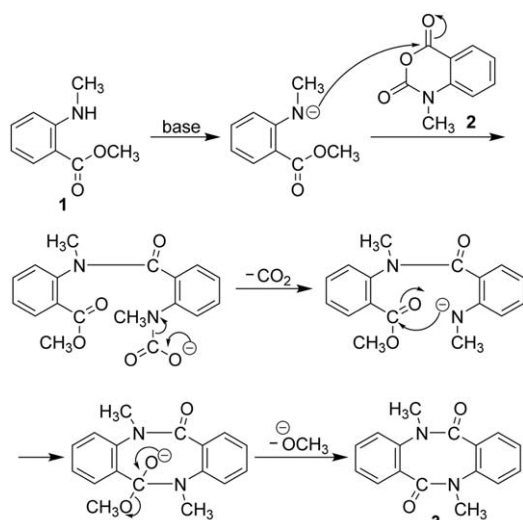
**INTRODUCTION** Synthesis of ladder polymers generally requires the construction of two bonds between monomer units. When the two bonds are simultaneously assembled by a concerted reaction, as in the case of the polymerization of bisepoxytetrahydroanthracene monomers<sup>1</sup> or ipitycene monomers<sup>2–4</sup> by a Diels–Alder reaction, defect-free ladder polymers can be obtained. A fully unsaturated ladder polymer has been synthesized using this method.<sup>5</sup> Recently, ladder polymers with benzocyclobutene backbones were synthesized via palladium catalyzed annulation.<sup>6</sup> Other than concerted reactions, a ladder structure can be constructed in a stepwise manner. For instance, ladder-type conjugated polymers have been synthesized using intramolecular Friedel–Crafts alkylation,<sup>7–14</sup> imine bridge-formation reactions,<sup>15,16</sup> and Bischler–Napieralski reaction<sup>17</sup> between monomer units of linear polyarylenes. This method was also applied to the synthesis of ladder polymers containing phenylene sulfide,<sup>18,19</sup> arylene ether,<sup>20</sup> and phenoxathiine<sup>21</sup> structures.

Aiming to synthesize ladder-type aromatic polyamides, we studied the reaction between *N*-methylantranilic acid methyl

ester (**1**) and *N*-methyisatoic anhydride (**2**) in the presence of a strong base as a model reaction and observed that the use of lithium hexamethyldisilazide (LiHMDS) as a base resulted in exclusive formation of two amide linkages successively between the two benzene rings to afford **3** (Scheme 1).<sup>22</sup> For the synthesis of ladder polymers using this reaction, the polymerization of 4,6-diaminoisophthalic acid monomers **4** bearing an anthranilic acid ester moiety and an isatoic anhydride moiety was investigated. In the presence of LiHMDS, the polymerization of **4** proceeded to yield polyamides with moderate molecular weight ( $M_n = 3350$ ,  $M_w = 6760$ ). However, the matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrum suggested that the polymer was composed primarily of linear and cyclized compounds and did not exhibit a ladder structure.<sup>23</sup> Because the positions *para* to the electron-donating nitrogen atoms of **4** are substituted by electron-withdrawing carbonyl groups, the nucleophilicity of the amino nitrogens and the electrophilicity of the carbonyl carbons are both weakened owing to the resonance effect shown in Scheme

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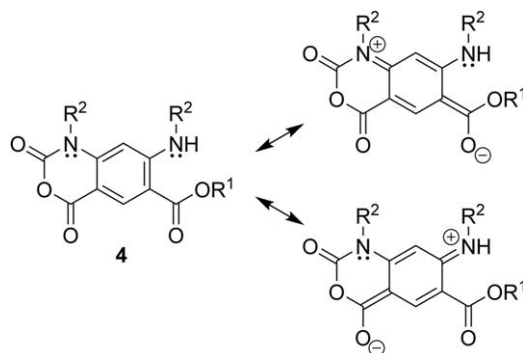
**SCHEME 1** Model reaction of **1** and **2**.

**2**, which might impede the polymerization. We expect that if the two nitrogen atoms as well as two carbonyl carbons are positioned *para* to one another, the nucleophilicity of the amino nitrogens and the electrophilicity of carbonyl carbons should increase, and the polymerization of such a monomer will afford higher molecular weight products. Herein, we report the polymerization of 2,5-diaminoterephthalic acid-type methyl ester monomers **5** and phenyl ester monomer **6** for the synthesis of ladder-type polyamide **7** (Scheme 3). We first tried the polymerization of *N*-octyl methyl ester monomer **5**, and polymers with moderate molecular weight were obtained. In this polymerization, the methoxide anion eliminated during the second amide-linkage formation was thought to disturb the polymerization. To reduce the nucleophilicity of the eliminated anion, methyl ester of **5** was changed into phenyl ester, and synthesis and polymerization of phenyl ester monomer **6a** was investigated. The polymerization of **6b** having a branched alkyl chain was also examined.

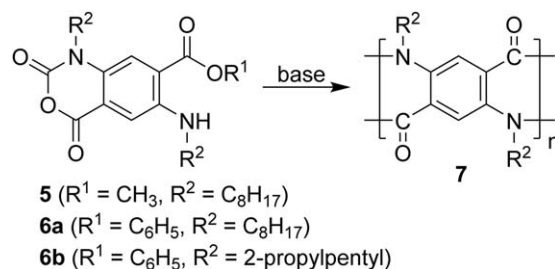
## EXPERIMENTAL

### Reagents and Methods

Commercially available dehydrated tetrahydrofuran (THF, stabilizer-free, Kanto, and super dehydrated, Wako), *N,N,N',N'*-



**SCHEME 2** Substituent effects of monomer **4**.

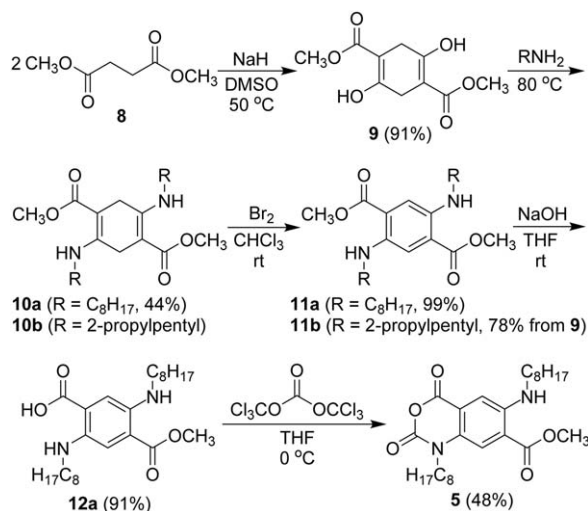


**SCHEME 3** Polymerization of monomer **5** and **6** for the synthesis of ladder polymer **7**.

dimethylformamide (DMF, super dehydrated, Wako), and dimethyl sulfoxide (DMSO, super dehydrated, Wako) were used as dry solvents. LiHMDS (1.0 mol/L solution in THF, Aldrich), sodium hexamethyldisilazide (NaHMDS, 1.0 mol/L solution in THF, Aldrich), potassium hexamethyldisilazide (KHMDS, 0.5 mol/L solution in toluene, TCI), 1-*tert*-butyl-2,2,4,4,4-pentakis(dimethylamino)-2 $\Lambda^5$ ,4 $\Lambda^5$ -catenadi(phosphazene) ( $P_2$ -*t*-Bu, 2.0 mol/L solution in THF, Aldrich), and 1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)phosphoranylideneamino]-2 $\Lambda^5$ ,4 $\Lambda^5$ -catenadi(phosphazene) ( $P_4$ -*t*-Bu, 0.8 mol/L solution in hexane, Aldrich) were used as received. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) and hexamethylphosphoric triamide (HMPA) were purified by distillation before use. Column chromatography was performed on silica gel (Kieselgel 60, 70–230, and 230–400 mesh, Merck, and neutral silica gel 60N, 63–210  $\mu\text{m}$ , Kanto Chemical) with a specified solvent. The detailed procedures for the synthesis of monomers **5** and **6** are described in the Supporting Information. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were obtained on JEOL ECA-500 and ECA-600 spectrometers at 23 °C unless otherwise specified. The internal standards of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were tetramethylsilane (0.00 ppm) and the midpoint of  $\text{CDCl}_3$  (77.0 ppm) in  $\text{CDCl}_3$ , respectively, as well as the midpoints of DMSO (2.50 ppm for  $^1\text{H}$  and 39.50 ppm for  $^{13}\text{C}$  NMR) in  $\text{DMSO}-d_6$ . Infrared (IR) spectra were recorded on a JASCO FT/IR-410 and FT/IR-470 plus. Gel permeation chromatography (GPC) profiles were obtained on a Shodex GPC-101 equipped with Shodex UV-41, Shodex RI-71S using two Shodex KF-804L columns, and a TOSOH HLC-8220 GPC unit using two TSKgel Multipore  $\text{H}_{\text{XL}}$ -M columns. THF was used as an eluent, and calibration was conducted using polystyrene standards. Isolation of polymer was conducted with a Japan Analytical Industry LC-908 Recycling Preparative HPLC unit (eluent:  $\text{CHCl}_3$ ) using two TSK gel columns (2  $\times$  G2000 $\text{H}_{\text{HR}}$ -M), and LC-9201 Recycling Preparative HPLC unit (eluent:  $\text{CHCl}_3$ ) using two JAIGEL columns (1H and 2H). MALDI-TOF mass spectra were recorded on a Shimadzu Biotech Axima CFRplus in the linear and reflectron modes using a laser ( $\lambda = 337 \text{ nm}$ ). The irradiation targets were prepared using THF as a solvent and 1,8,9-anthracene-triol (dithranol) as a matrix, with sodium or potassium trifluoroacetate as cationization salts. Electrospray ionization (ESI) mass spectra were recorded on a Thermo Fisher Scientific Q Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometer.

### General Procedure of Polymerization

All glass apparatus was dried before use. Addition of reagents into the reaction flask was conducted via a syringe



SCHEME 4 Synthesis of monomer 5.

from the three-way stopcock with a stream of nitrogen. A round-bottomed flask equipped with a three-way stopcock was heated under reduced pressure and then cooled to room temperature under an argon atmosphere. The monomer **6a** (104 mg, 0.20 mmol) was placed in the flask, and the atmosphere in the flask was replaced with argon. Into the flask was added THF (0.6 mL), and the solution was stirred at 50 °C. A 1.0-mol/L solution of LiHMDS in THF (0.20 mL, 0.20 mmol) was added dropwise via a syringe, and the mixture was stirred at 50 °C for 48 h. After the reaction mixture was cooled to room temperature, an aqueous saturated ammonium chloride solution was added, and the mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with water and brine, dried over anhydrous  $\text{MgSO}_4$ , and concentrated under reduced pressure to yield a crude product (84.4 mg) as a brown solid.  $M_n = 4300$ ,  $M_w = 10,010$ .

## RESULTS AND DISCUSSION

### Synthesis of Monomers

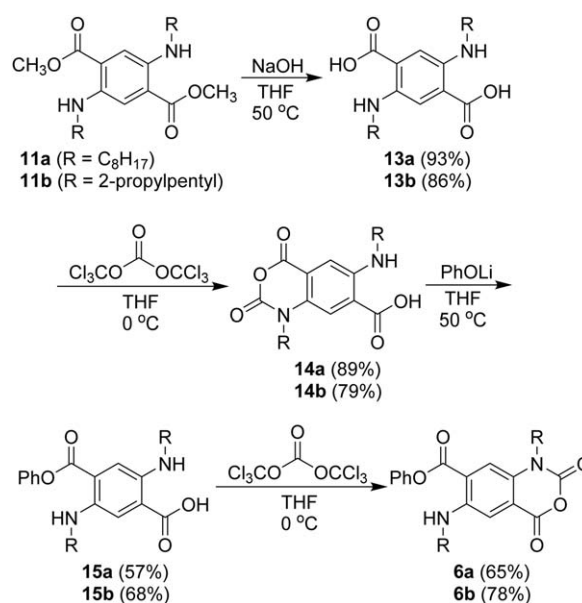
Dimethyl ester of 2,5-bis(octylamino)terephthalic acid was synthesized according to the reported procedure with some modifications (Scheme 4).<sup>24</sup> Treatment of dimethyl succinate (**8**) with NaH in DMSO afforded **9** via the Claisen condensation.<sup>25</sup> The reaction of **9** with octyl amine afforded amine **10a** accompanied by a small amount of oxidized product **11a** (4%). The 1,4-cyclohexadiene structure of amine **10a** was oxidized with bromine in chloroform to yield aromatized **11a**. Selective hydrolysis of one of the two methyl ester linkages of **11a** by sodium hydroxide in THF at 0 °C followed by treatment of the obtained carboxylic acid **12a** with triphosgene yielded the monomer **5**.<sup>26</sup>

Compound **11b** having a 2-propylpentyl side chain was synthesized in the same manner as **11a** (Scheme 4). The syntheses of phenyl ester monomer **6a** and **6b** were conducted according to Scheme 5. Complete hydrolysis of the dimethyl ester **11** with sodium hydroxide at 50 °C afforded dicarboxylic acid **13**, which was treated with triphosgene to give **14**.

The esterification of **14a** using phenol and a condensation agent such as 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide did not afford the phenyl ester **6a** but resulted in dimerization of **14a**. Therefore, the phenyl ester moiety was constructed by the reaction of **14** with lithium phenoxide and the obtained **15** was treated with triphosgene to afford the monomers **6a** and **6b**.

### Polymerization of Methyl Ester Monomer 5

To conduct the polymerization of **5** under optimized conditions determined by the model reaction,<sup>22</sup> a THF solution of LiHMDS (1.0 equivalent) was added to a solution of **5** in a mixture of THF and TMEDA<sup>27</sup> at 0 °C and the reaction mixture was warmed to room temperature. Precipitates were observed at 0 °C and dissolved gradually at room temperature. The precipitates might be lithium salt of carbamic acid formed by the nucleophilic attack of the amide anion of the monomer on the carbonyl carbon of isatoic anhydride moiety of another monomer, followed by cleavage of oxygen-carbonyl bond of isatoic anhydride moiety. Eventually, the reaction mixture became a clear solution. Polymerization at room temperature for 5 h yielded a polymer with  $M_n = 3070$  and  $M_w = 3600$  (Table 1, entry 1). The GPC profiles of the reaction mixture revealed that the growth of the polymerization ceased at 1 h and a small amount of the monomer **5** remained unreacted (Supporting Information Fig. S1). The MALDI-TOF mass spectra of the products (Supporting Information Fig. S3) indicated that the product contained **16**, which is a linear oligoamide with an amide terminal unit. This compound is thought to be formed by the reaction of the isatoic anhydride terminal unit of the growing oligomers with the bis(trimethylsilyl)amide anion of LiHMDS, followed by hydrolysis during the work-up (Scheme 6). The polymerization under diluted conditions (entry 2) and that with HMPA instead of TMEDA as an additive (entry 3) also led to similar results.

SCHEME 5 Synthesis of monomers **6a** and **6b**.

**TABLE 1** Polymerization of **5**<sup>a</sup>

Entry	Base	Solvent (mL)	Additive (mL)	Time (h)	$M_n^b$	$M_w^b$
1	LiHMDS	THF (0.6)	TMEDA (0.17)	5	3070	3600
2	LiHMDS	THF (1.2)	TMEDA (0.17)	24	2820	3380
3	LiHMDS	THF (0.2)	HMPA (0.5)	24	2120	2410
4	P <sub>2</sub> -t-Bu	THF (0.4)	–	24	1990	2680
5	P <sub>4</sub> -t-Bu	THF (0.2)-hexane (0.2) <sup>c</sup>	–	24	2230	2870

<sup>a</sup> The polymerization of **5** (0.20 mmol) was conducted with a base (1.0 equivalent) at room temperature.

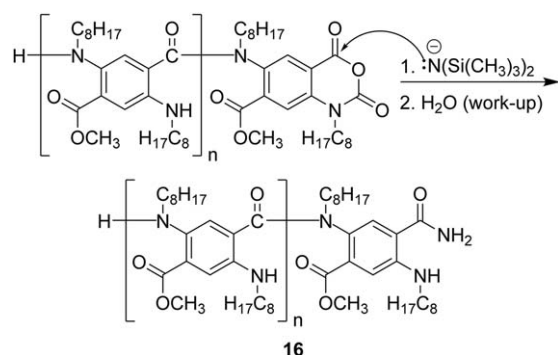
<sup>b</sup> Determined by GPC based on polystyrene standards (eluent: THF).

<sup>c</sup> Hexane was incorporated as a reaction solvent because hexane solution of P<sub>4</sub>-t-Bu was used.

Because the formation of **16** indicates that the nucleophilic attack of the bis(trimethylsilyl)amide anion disturbed the polymerization, we changed the base from LiHMDS to a phosphazene base such as P<sub>2</sub>-t-Bu and P<sub>4</sub>-t-Bu, which are known as strong but less nucleophilic bases.<sup>28</sup> Polymerization with P<sub>2</sub>-t-Bu afforded a product with  $M_n = 1990$  and  $M_w = 2680$  (entry 4), and the use of P<sub>4</sub>-t-Bu led to similar results (entry 5). In the polymerization with P<sub>2</sub>-t-Bu, almost complete conversion of the monomer, indicated by GPC trace of the product (Supporting Information Fig. S2), reveals that P<sub>2</sub>-t-Bu functioned as a base more efficiently than LiHMDS in this polymerization. However, the MALDI-TOF mass spectra of the product (Supporting Information Fig. S4) showed the signals with mass/charge values corresponding to not only the linear trimer **17** and its hydrolyzed product **18** but also the methyl ester-terminated **19** (Fig. 1). The formation of **19** suggests that the use of P<sub>4</sub>-t-Bu as a base induced the second amide formation more efficiently as compared to the case of LiHMDS, but methoxide anion eliminated during the second amide-linkage formation, as shown in Scheme 1, attacked the isotactic anhydride terminal unit of the oligomer to impede the polymerization. We thought the use of phenyl ester monomer could prevent the decomposition of the isotactic anhydride terminal unit because the nucleophilicity of the phenoxide anion is much lower than that of the methoxide anion. Therefore, we decided to examine the polymerization of the phenyl ester monomers **6a** and **6b**.

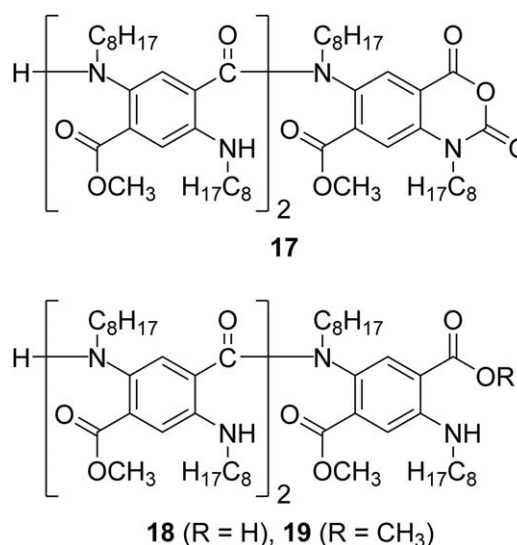
#### Polymerization of Phenyl Ester Monomer **6a** and **6b**

The *N*-octyl phenyl ester monomer **6a** was polymerized with 1.0 equivalent of LiHMDS and 5.0 equivalents of TMEDA in

**SCHEME 6** Formation of amide terminal polyamide **16**.

THF at 0 °C. As in the case of the polymerization of the methyl ester monomer **5**, precipitates were formed when a solution of **6a** in THF was added to a solution of LiHMDS and TMEDA in THF. The precipitates gradually dissolved and disappeared at a later stage of the polymerization. After the reaction at 0 °C for 48 h, the polymer with  $M_n = 2480$  and  $M_w = 3230$  was obtained (Table 2, entry 1). The GPC elution curve of the product showed that a small amount of the monomer remained unreacted [Fig. 2(a)].

To estimate the degree of second amide-linkage formation, we used compound **20** as a model of linear structure in which two benzene rings are connected with one amide linkage and compound **21** as a model of the ladder structure in which the second amide linkage was formed, and compared the <sup>1</sup>H NMR spectra of these compounds with the polymer obtained (Fig. 3). As shown in Figures 3(a,b), when the <sup>1</sup>H NMR spectrum was measured in 1,1,2,2-tetrachloroethane-*d*<sub>2</sub> at 100 °C, one of two methylene protons next to the amide nitrogen atom of **21** (H<sub>c</sub>) was observed separately from N-CH<sub>2</sub> of **20** (H<sub>a</sub> and H<sub>b</sub>). On the basis of these results, in the <sup>1</sup>H NMR spectra of the polymer **22** composed of ladder and linear structures measured under the same conditions,

**FIGURE 1** Chemical structure of oligomers obtained by the polymerization of **5** with P<sub>2</sub>-t-Bu.

**TABLE 2** Polymerization of **6a**<sup>a</sup>

Entry	Base	Solvent (mL)	Additive	Temperature (°C)	$M_n^b$	$M_w^b$	Ladder Ratio (%) <sup>c</sup>
1	LiHMDS	THF (0.8)	TMEDA	0	2480	3230	26
2	LiHMDS	THF (0.8)	TMEDA	rt	3060	4350	24
3	LiHMDS	THF (0.8)	TMEDA	50	3370	5360	29
4	LiHMDS	THF (0.8)	–	0	3020	3980	24
5 <sup>d</sup>	LiHMDS	THF (0.8)	–	rt	3580	5200	29
6	LiHMDS	THF (0.8)	–	50	4300	10,010	57
7	LiHMDS	HMPA (0.6)-THF (0.2) <sup>e</sup>	–	50	2600	4650	51
8	LiHMDS	DMF (0.6)-THF (0.2) <sup>e</sup>	–	50	2580	4250	58
9	LiHMDS	1,4-Dioxane (0.6)-THF (0.2) <sup>e</sup>	–	50	3760	7180	nd <sup>f</sup>
10	LiHMDS	Toluene (0.6)-THF (0.2) <sup>e</sup>	–	50	2870	4000	27
11	NaHMDS	THF (0.8)	–	50	3290	4700	32
12	KHMDS	THF (0.6)-toluene (0.4) <sup>e</sup>	–	50	3860	5960	26
13	P <sub>2</sub> -t-Bu	THF (0.8)	–	50	1180	1340	45
14	P <sub>4</sub> -t-Bu	THF (0.6)-hexane (0.25) <sup>e</sup>	–	50	2000	2910	75

<sup>a</sup> The polymerization of **6a** (0.20 mmol) was conducted with a base (1.0 equivalent) and an additive (5.0 equivalent) for 48 h.

<sup>b</sup> Determined by GPC based on polystyrene standards (eluent: THF).

<sup>c</sup> Determined by <sup>1</sup>H NMR in 1,1,2,2-tetrachloroethane-*d*<sub>2</sub> at 100 °C.

<sup>d</sup> The reaction time was 53 h.

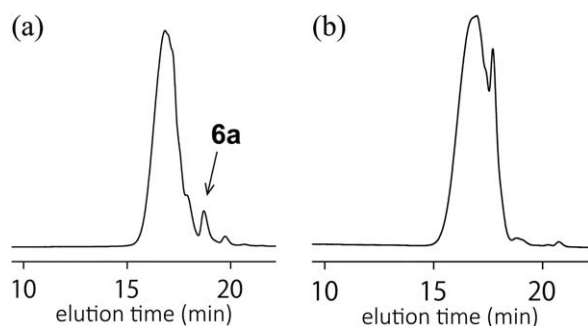
<sup>e</sup> Derived from a solvent of the base.

<sup>f</sup> The value could not be determined because the products showed low solubility in chloroform and could not be purified by recycling preparative HPLC (eluent: chloroform).

two of four N–CH<sub>2</sub> protons of the ladder structure (H<sub>γ</sub>) would appear in area A shown in Figure 3(c); the other two protons (H<sub>δ</sub>) as well as the N–CH<sub>2</sub> protons of the linear structure (H<sub>α</sub> and H<sub>β</sub>) would appear in area B. Therefore, the ratio of second amide-linkage formation, defined as the ladder ratio, can be determined using the integral values of area A (Int<sub>A</sub>) and area B (Int<sub>B</sub>) by the following equation:

$$\text{ladder ratio(\%)} = \frac{x}{x+y} \times 100 = \frac{\text{Int}_A}{\text{Int}_A + (\text{Int}_B - \text{Int}_A)/2} \times 100. \quad (1)$$

In eq 1, *x* and *y* are the number of ladder and linear units in **22**, respectively. According to this equation, the ladder ratio value of the polymer obtained by this polymerization was calculated to be 26%.

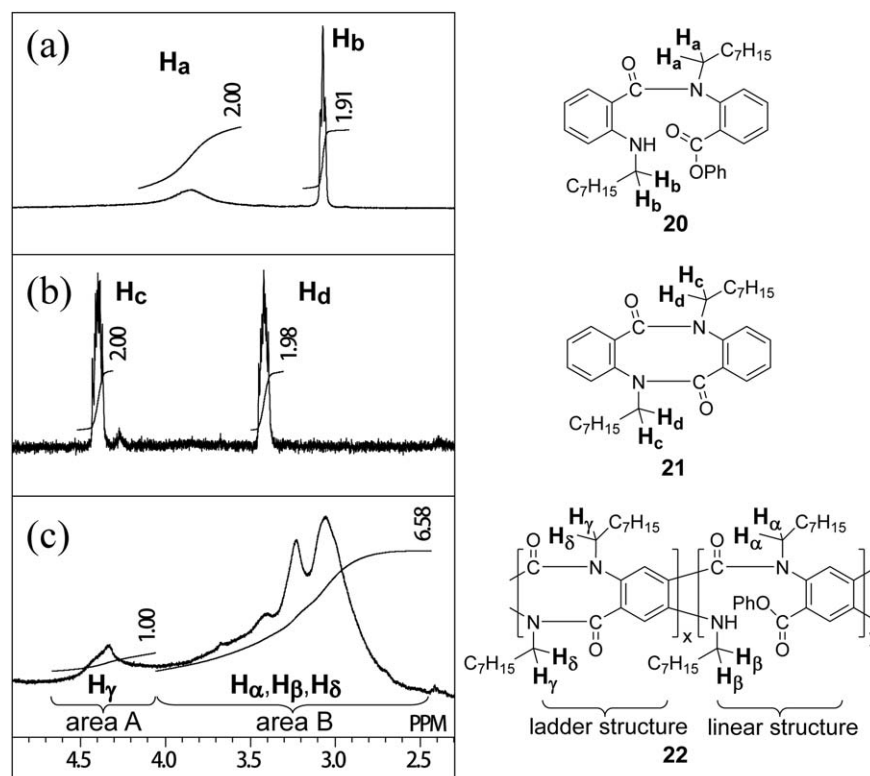


**FIGURE 2** GPC profiles of the crude products obtained by (a) the polymerization of **6a** with 1.0 equivalent of LiHMDS in the presence of 5.0 equivalents of TMEDA in THF at 0 °C for 48 h, and (b) the polymerization of **6b** with 1.0 equivalent of LiHMDS in THF at 50 °C for 48 h.

Increasing the reaction temperature increased the molecular weight of the products with almost the same value of the ladder ratio (entries 2 and 3). Furthermore, polymerization without TMEDA afforded the polymers with higher molecular weight at each reaction temperature (entries 4–6). In particular, a polymer with  $M_n = 4300$ ,  $M_w = 10010$ , and ladder ratio = 57% was obtained by the polymerization without TMEDA at 50 °C (entry 6).

When the polymerization was conducted in THF as described above, the precipitate formation was observed every time at an early stage of polymerization. We thought that the precipitate formation would disturb the growth of polymerization to reduce the molecular weight and ladder ratio of the polymer. To conduct the polymerization without the precipitation, the polymerization solvent was changed. In each polymerization described below, a small amount of THF was incorporated as a solvent because we purchased 1.0 mol/L THF solution of LiHMDS and used it as a base. Polymerization in HMPA (entry 7) and DMF (entry 8) proceeded without precipitation and that in 1,4-dioxane (entry 9) and toluene (entry 10) resulted in the formation of a precipitate. In all polymerizations, however, the molecular weights of the obtained polymers were lower compared with the polymerization in THF.

Next, we investigated the effect of base on this polymerization. First, the counter cation of LiHMDS was changed and the polymerization was conducted with NaHMDS and KHMDS. However, the molecular weight and the ladder ratio of the obtained polymers were decreased (entries 11 and 12). Polymerization with a phosphazene base afforded a polymer with high ladder ratio (entries 13 and 14). In



**FIGURE 3**  $^1\text{H}$  NMR spectra of (a) linear model compound **20**, (b) ladder model compound **21**, and (c) the product **22** obtained by the polymerization of **6a** with 1.0 equivalent of LiHMDS with 5.0 equivalents of TMEDA in THF at 0 °C for 48 h. The spectra were observed in 1,1,2,2-tetrachloroethane- $d_2$  at 100 °C.

particular, ladder ratio of the polymer obtained by the polymerization with  $\text{P}_4\text{-t-Bu}$  was 75%. However, as in the case of the polymerization of **5**, the molecular weights of the polymers were very low.

As described above, the polymer with the highest molecular weight and ladder ratio was obtained when the polymerization of **6a** was conducted with 1.0 equivalent of LiHMDS in THF at 50 °C, despite the precipitate formation at an early stage of polymerization. To conduct the polymerization under these conditions without the precipitation, we used the monomer **6b**, the branched *N*-alkyl chain of which was expected to increase the solubility of the polymer. When **6b** was polymerized in the presence of LiHMDS in THF, precipitation was not observed during the polymerization. However, the molecular

weight ( $M_n = 2390$ ,  $M_w = 3600$ ) and the ladder ratio (44%) of the polymer were low compared with the polymerization of **6a** (Table 3, entry 1). The GPC elution curve of the product by the polymerization of **6b** in THF showed a shoulder at the lower molecular weight region [Fig. 2(b)]. We isolated the products corresponding to the low-molecular-weight shoulder peak by recycling preparative HPLC. The ESI mass spectroscopy analysis revealed that the compounds contained phenyl ester-terminated trimer **23** and **24** or cyclic trimer **25** (Supporting Information Fig. S5; Fig. 4). However, the complex  $^1\text{H}$  NMR spectra indicate that the main component was **23** and/or **24**, not **25**, because symmetrical structure of **25** should result in a simple  $^1\text{H}$  NMR spectrum. As in the case of the formation of **19** in the polymerization of methyl ester monomer **5**, the formation of **23** or **24** suggests that the phenoxide anion

**TABLE 3** Polymerization of **6b**<sup>a</sup>

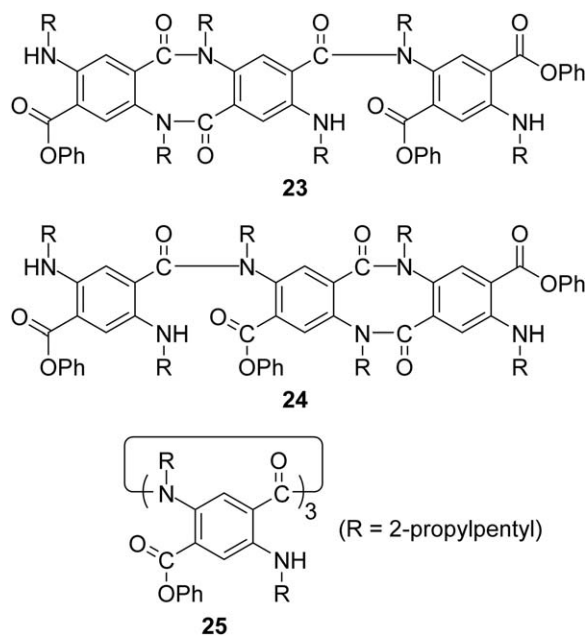
Entry	Base	Solvent (mL)	$M_n^b$	$M_w^b$	Ladder Ratio (%) <sup>c</sup>
1	LiHMDS	THF (0.8)	2390	3600	44
2	LiHMDS	HMPA (0.6)-THF (0.2) <sup>d</sup>	1540	2030	62
3	LiHMDS	1,4-Dioxane (0.6)-THF (0.2) <sup>d</sup>	2840	3910	21
4	LiHMDS	Toluene (0.6)-THF (0.2) <sup>d</sup>	2650	3830	27
5	$\text{P}_4\text{-t-Bu}$	THF (0.8)	1170	1370	74

<sup>a</sup> The polymerization of **6b** (0.20 mmol) was conducted with a base (1.0 equivalent) at 50 °C for 48 h.

<sup>b</sup> Determined by GPC based on polystyrene standards (eluent: THF).

<sup>c</sup> Determined by  $^1\text{H}$  NMR in 1,1,2,2-tetrachloroethane- $d_2$  at 100 °C.

<sup>d</sup> Derived from a solvent of the base.



**FIGURE 4** Chemical structure of phenyl ester-terminated trimer **23** and **24** and cyclic trimer **25**.

still reacted with the isatoic anhydride terminal unit of the growing oligomer during the formation of second amide-linkage, despite its decreased nucleophilicity as compared to methoxide anion. As shown in Figure 2(a), the GPC elution curve of the product obtained by the polymerization of **6a** under the same conditions did not show such a shoulder at the lower molecular weight region, indicating that the side reaction which gave the by-products similar to **23** and **24** did not occur in the polymerization of **6a**. Therefore, the steric hindrance of the branching *N*-alkyl unit of **6b** would decrease the rate of polymerization of **6b**, and the nucleophilic attack of the phenoxide anion on the isatoic anhydride unit might compete with the polymerization of **6b**. The decrease in the polymerization rate by the branching *N*-alkyl side chain was reported in the copolymerization of 4-aminobenzoic acid esters with linear and branched *N*-alkyl units.<sup>29</sup> In the polymerization of **6b**, a change in solvent from THF to HMPA, 1,4-dioxane, or toluene did not improve the polymerization results (entries 2–4). Similar to the polymerization of **6a**, the use of  $P_4$ -*t*-Bu as a base resulted in a formation of the polymer with low molecular weight but high ladder ratio (entry 5). This result is also supported by the decomposition of the isatoic anhydride unit by the phenoxide anion, because the concentration of the phenoxide anion would increase as the ladder ratio of the product increases, which might promote the reaction between the phenoxide anion and isatoic anhydride unit.

## CONCLUSIONS

For the synthesis of ladder-type polyamide **7**, we prepared 2,5-diaminoterephthalic acid-type monomers **5** and **6** and optimized the reaction conditions for their polymerization. The MALDI-TOF mass spectrometric analysis of the product obtained by the polymerization of the methyl ester monomer

**5** with LiHMDS indicated that the bis(trimethylsilyl)amide anion attacked the isatoic anhydride moiety of the growing oligomer end. Furthermore, in the polymerization with phosphazene base, nucleophilic attack of the methoxide anion formed during the second amide-linkage formation was also suggested. To reduce this side reaction, the polymerization of phenyl ester monomer **6a** was investigated and the polymer with highest molecular weight ( $M_n = 4300$  and  $M_w = 10,010$ ) and a high ladder ratio (57%) was obtained by polymerization with 1.0 equivalent of LiHMDS in THF at 50 °C. In this polymerization, the formation of a precipitate was observed at an early stage. Use of **6b** possessing branched *N*-alkyl chains as a monomer resulted in polymerization without precipitation, but the molecular weight and ladder ratio of the obtained polymer were low. The ESI mass spectrometric analysis of the by-product suggested that the nucleophilic attack of the phenoxide anion at the isatoic anhydride moiety disturbed the polymerization. This side reaction might be suppressed by a two-stage polymerization, in which a linear polyamide is synthesized at the first stage, and then the second amide linkage is constructed at the next stage. Efforts in this direction are currently ongoing.

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