Polymer Journal (2015) 47, 348–351

www.nature.com/pj

NOTE

Polymerization of 4,6-diaminoisophthalic acid-type monomers bearing anthranilic acid ester and isatoic anhydride moieties

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Polymer Journal (2015) **47,** 348–351; doi:10.1038/pj.2014.105; published online 17 December 2014

INTRODUCTION

Ladder polymers have received attention because of their superior properties as compared with non-ladder polymers. For example, the phenoxathiinium-type ladder polymers show higher stability against thermolysis than corresponding non-ladder polymers.[1] In addition, the study of electron mobility in field-effect transistors demonstrates a large enhancement in carrier mobility in ladder-type poly(benzobisimidazobenzophenanthroline) compared with its non-ladder analog.[2] Many types of ladder polymers have been synthesized via bond formation between repetitive units of a linear polymer. In this case, the obtained ladder polymers sometimes contain defects owing to incomplete formation of the second bond. In contrast, defect-free ladder polymers have been synthesized using concerted reactions, particularly the Diels–Alder reaction.[3–6]

In the course of our study of the controlled synthesis of *N*-substituted aromatic polyamides,[7,8] we have been interested in the synthesis and properties of aromatic ladder polyamides, in which two benzene rings are connected by two amide linkages. To synthesize this type of ladder polymer, we investigated the condensation reaction between *N*-alkylanthranilic acid methyl ester and *N*-alkylisatoic anhydride in the presence of a strong base, and developed a reaction that constructed two amide linkages successively between two benzene rings.[9] The use of lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS) as a base and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as an additive in the model reaction resulted in high yield of the target compound. For the synthesis of a ladder polyamide using this reaction between A_2- and B_2-type monomers, we designed the monomers **1** and **2**; their polymerization was expected to afford the aromatic ladder polyamide **3** (Scheme 1). Octyl unit was chosen as a side chain to make the polymer soluble. Similarly, monomer **4** was designed as an AB-type monomer, whose polymerization might also give **3**. In this report, we describe the synthesis and polymerization studies of these monomers.

EXPERIMENTAL PROCEDURE

Materials

Commercially available dehydrated tetrahydrofuran (THF, stabilizer free, Kanto Chemical, Tokyo, Japan) was used as a dry solvent. TMEDA (TCI, Tokyo, Japan) was distilled before use. LiHMDS (1.0 M solution in THF, Aldrich, St Louis, MO, USA) was used as received. 4,6-Dinitroisophthalic acid (**5**) was synthesized according to the literature.[10] Detailed procedures for the synthesis of monomers **1**, **2**, and **4** are described in the Supplementary Information. Column chromatography was performed on silica gel (Kieselgel 60, 70–230 and 230–400 mesh, Merck, Darmstadt, Germany) with a specified solvent.

Measurements

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained on JEOL ECA-500 and ECA-600 spectrometers at 23 °C. The internal standards of the ^{1}H and ^{13}C NMR spectra were tetramethylsilane (0.00 p.p.m.) and the midpoint of $CDCl_3$ (77.0 p.p.m.) in $CDCl_3$, respectively, as well as the midpoints of dimethyl sulfoxide (DMSO, 2.50 p.p.m. for ^{1}H and 39.50 p.p.m. for ^{13}C NMR) in DMSO-d_6. Infrared (IR) spectra were recorded on a JASCO FT/IR-410 (JASCO, Tokyo, Japan). Size exclusion chromatography (SEC) profiles were obtained on a Shodex GPC-101 (Shoko Scientific, Yokohama, Japan) equipped with Shodex UV-41, Shodex RI-71S and two Shodex KF-804L columns (bead size = 7 μm, pore size = 200 Å). THF was used as the eluent (temperature = 40 °C, flow rate = 2 ml min^{-1}), and calibration was carried out using polystyrene standards. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectra were recorded on a Shimadzu Biotech (Kyoto, Japan) Axima CFRplus in the linear and reflectron modes using a laser (λ = 337 nm). The irradiation targets were prepared using THF as a solvent and 1,8,9-anthracenetriol (dithranol) as a matrix with potassium trifluoroacetate as a cationization salt.

Polymerization of 1 and 2

A solution of LiHMDS in THF (1.0 mol l^{-1}, 0.20 ml, 0.20 mmol) was stirred in a reaction tube at 0 °C under an argon atmosphere. A solution of **1** (44.9 mg, 0.10 mmol) and **2** (47.3 mg, 0.10 mmol) in dry THF (1.0 ml), followed by TMEDA (0.15 ml, 1.0 mmol), was then added successively via syringes under a stream of nitrogen. The mixture was stirred at 0 °C for 1.5 h, and the tube was

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Received 20 August 2014; revised 17 October 2014; accepted 18 October 2014; published online 17 December 2014

degassed by means of three freeze-pump-thaw cycles. The mixture was subsequently frozen by cooling with liquid nitrogen, and the pressure inside the reaction tube was reduced. After the tube was sealed, the reaction mixture was heated at 70 °C for 1 h and then cooled to room temperature. A saturated aqueous solution of ammonium chloride was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to give a yellow syrup (41.0 mg, 98%) as a product. $M_n = 2040$, $M_w = 3020$ (SEC).

Polymerization of 4

A solution of **4** (91.9 mg, 0.20 mmol) and TMEDA (0.17 ml, 1.1 mmol) in dry THF (0.2 ml) was stirred in a reaction tube at 0 °C under an argon atmosphere, and a solution of LiHMDS in THF (1.0 mol l^{-1}, 0.20 ml, 0.20 mmol) was added dropwise via syringes under a stream of nitrogen. Following that, the tube was sealed and the reaction mixture was heated at 50 °C for 20.5 h and then cooled to room temperature. After a saturated aqueous solution of ammonium chloride was added, the mixture was extracted with ethyl acetate, and the organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to give a yellow syrup (88 mg, quantitative) as a product. $M_n = 3350$, $M_w = 6760$ (SEC).

RESULTS AND DISCUSSION

Monomer synthesis

The monomers **1**, **2** and **4** were synthesized as shown in Scheme 2. Reduction of 4,6-dinitroisophthalic acid (**5**)[10] under catalytic hydrogenation conditions afforded the diamine **6**, which was treated with triphosgene[11] in 1,4-dioxane to give **7**. After solvolysis of **7** in methanol in the presence of triethylamine, the introduction of octyl units into the two amino groups of the resulting diester **8** by reductive amination of octanal with sodium triacetoxyborohydride[12] gave the A_2-type monomer **1**. When **1** was treated with 0.33 equivalent of triphosgene at 90 °C for 1 h, the AB-type monomer **4** was obtained selectively. In contrast, the reaction of **1** with 0.71 equivalent of triphosgene at 90 °C for 22 h afforded the B_2-type monomer **2** in high yield.

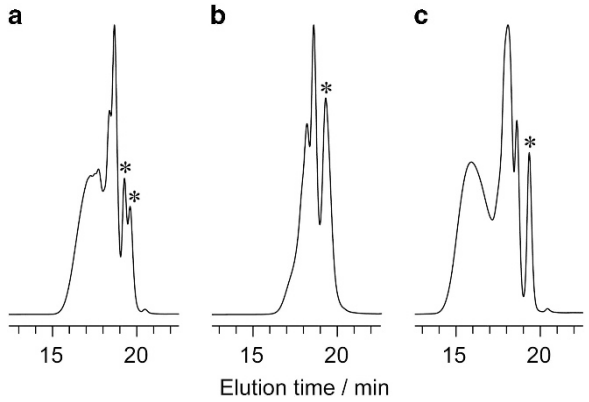
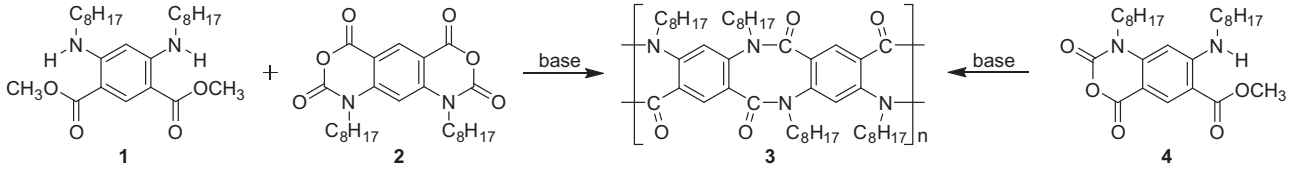
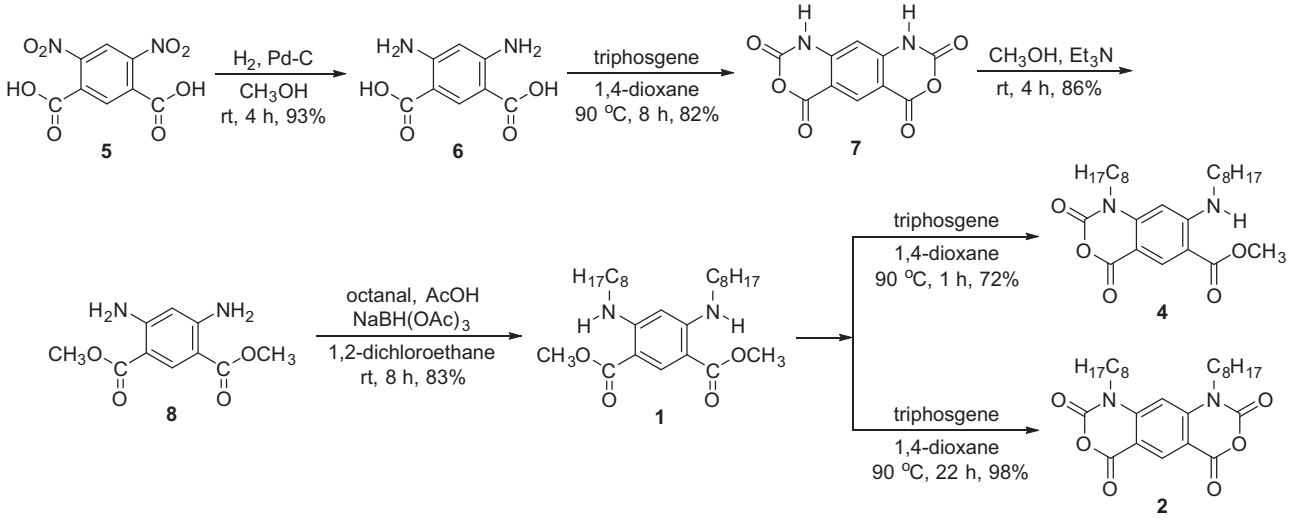


Figure 1 Size-exclusion chromatography profiles of the reaction products obtained by (**a**) the polymerization of **1** and **2** ($[\mathbf{1}]_0 = [\mathbf{2}]_0 = 0.074$ mol l^{-1}) with lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, 2.0 equivalents) in the presence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA, 10.0 equivalents) in tetrahydrofuran (THF) at 70 °C for 1 h, (**b**) the polymerization of **4** ($[\mathbf{4}]_0 = 0.086$ mol l^{-1}) with LiHMDS (1.0 equivalent) in the presence of TMEDA (5.0 equivalents) in THF at 70 °C for 48 h and (**c**) the polymerization of **4** ($[\mathbf{4}]_0 = 0.35$ mol l^{-1}) with LiHMDS (1.0 equivalent) in the presence of TMEDA (5.5 equivalents) in THF at 50 °C for 20.5 h. The peaks marked with an asterisk (*) correspond to the monomers.



Scheme 1 Synthesis of ladder polymer **3** by the polymerization of A_2- and B_2-type monomers (**1**, **2**) and AB-type monomer (**4**).



Scheme 2 Synthesis of monomers **1**, **2** and **4**.

Polymerization of A_2- and B_2-type monomers

Polymerization of **1** and **2** was carried out under the optimized conditions determined by the model reaction, using 2.0 equivalents of LiHMDS as a base in the presence of 10.0 equivalents of TMEDA in THF.[9] The reaction tube was sealed after the pressure inside the tube had been reduced, and the reaction mixture was heated at 70 °C for 1 h. SEC analysis of the reaction mixture revealed that the reaction almost ceased in 5 min despite incomplete consumption of the monomers, and an oligomeric product ($M_n = 2040$, $M_w = 3020$) was formed (Figure 1a). As shown in Figure 2a, the MALDI-TOF mass spectrum of the crude product showed molecular ion peaks whose *m*/*z* values agreed with the molecular weight of the linear-type products, such as $A-(BA)_n-A$ type oligomers **9** ($n = 1$–3) and an amide-terminated oligomer **10** (Figure 3). However, the molecular ion peaks corresponding to the ladder structure were not observed. The formation of the amide-terminated oligomer **10** suggests that bis(trimethylsilyl)amide anion not only functioned as a base but also attacked the isatoic anhydride moiety of the monomer **2** and/or the polymer end. To avoid the nucleophilic attack of the base, the base should be reacted with **1** before the addition of **2**. If an amide anion generated by the deprotonation of **1** attacks the ester moiety of another **1** molecule and an amide linkage forms, **1** may polymerize in the absence of **2**. Therefore, we first checked the self-polymerization ability of **1** in the presence of a base. When **1** was treated with 2.0 equivalents of LiHMDS in the presence of 10.0 equivalents of TMEDA in THF at 70 °C for 30 min, no reaction was observed, demonstrating that the treatment of **1** with a base does not induce polymerization. Addition of **2** to the deprotonated **1** induced polymerization at room temperature, but the reaction stopped before complete consumption of the monomers, and only oligomeric products ($M_n = 2290$, $M_n = 3040$) were obtained after reacting at room temperature for 63 h.

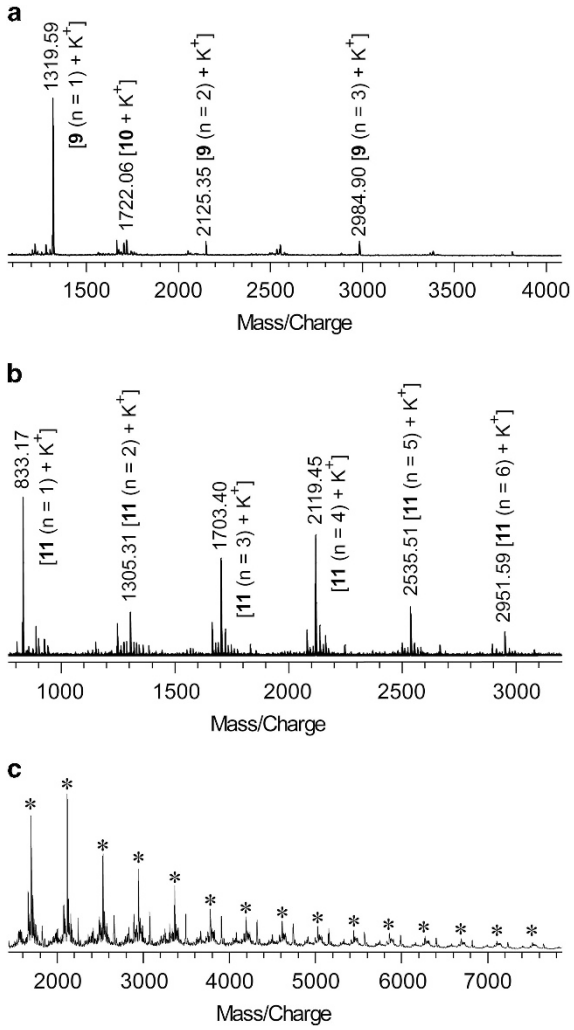


Figure 2 Matrix-assisted laser desorption ionization time-of-flight mass spectra of the reaction products obtained by (**a**) the polymerization of **1** and **2** ($[\mathbf{1}]_0 = [\mathbf{2}]_0 = 0.074\ \mathrm{mol\,l^{-1}}$) with lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, 2.0 equivalents) in the presence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA, 10.0 equivalents) in tetrahydrofuran (THF) at 70 °C for 1 h, and (**b** and **c**) the polymerization of **4** ($[\mathbf{4}]_0 = 0.35\ \mathrm{mol\,l^{-1}}$) with LiHMDS (1.0 equivalent) in the presence of TMEDA (5.5 equivalents) in THF at 50 °C for 20.5 h. The peaks marked with an asterisk (*) correspond to the cyclized product **11**. The measurements were carried out in the reflectron mode (**a** and **b**) and in the linear mode (**c**).

Polymerization of AB-type monomer

As in the case of the polymerization of the A_2- and B_2-type monomers, the AB-type methyl ester monomer **4** was polymerized with 1.0 equivalent of LiHMDS in the presence of 5.0 equivalents of TMEDA in THF at 70 °C for 48 h. The reaction proceeded, but the conversion of **4** was not completed and a low molecular weight-product ($M_n = 1660$, $M_w = 1950$) was obtained (Figure 1b). In order to polymerize **4** more efficiently, we examined the polymerization under various reaction conditions, and found that the polymerization of **4** under concentrated conditions (four times) at 50 °C proceeded smoothly with the efficient conversion of the monomer, yielding a higher molecular weight-product with a bimodal SEC elution curve (Figure 1c, $M_n = 3350$, $M_w = 6760$). When the product was analyzed by MALDI-TOF mass spectroscopy in the reflectron mode, the mass/charge values of the main peaks corresponded to potassium ion adducts of cyclized products **11** (Figure 2b). Furthermore, the linear mode MALDI-TOF mass analysis suggested that the product consisted of oligomers and polymers whose repeating unit corresponded to the linear-type polymer **12** with several terminal structures, as well as the

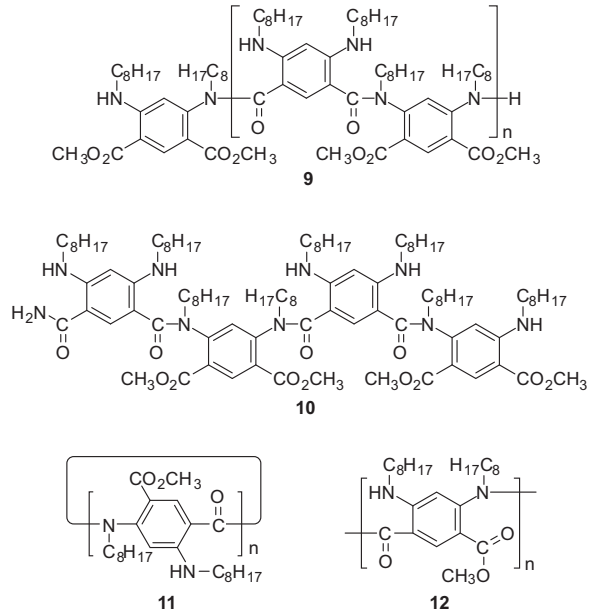


Figure 3 Proposed structures of the reaction products.

cyclized products **11** (Figure 2c). As in the case of the polymerization of the A_2- and B_2-type monomers **1** and **2**, products with the ladder-type structure were not detected by the MALDI-TOF mass analysis. In these polymerizations, the deprotonated amide ion of the monomer attacks the carbonyl group adjacent to the benzene ring at the isatoic anhydride moiety of another monomer, leading to the formation of an amide linkage and a carbamate ion.[9] If decarbonation of the carbamate ion occurs and the formed amide ion attacks the neighboring ester moiety, the ladder structure will be obtained. We believe that the electron-withdrawing carbonyl group at the para position of the nitrogen atom of **2** and **4** reduces the nucleophilicity of the amide ion formed by the decarbonation, retarding the formation of the ladder structure.

CONCLUSION

The A_2- and B_2-type monomers **1** and **2** and the AB-type monomer **4** were synthesized and their polymerization was conducted under the conditions determined by the model reaction for the ladder polymer. The polymerization of **1** and **2** afforded small molecular weight-products, but polymerization of **4** gave higher molecular weight-products ($M_n = 3350$, $M_w = 6760$). The MALDI-TOF mass analysis suggested that the higher molecular weight-products consisted of non-ladder type linear (**12**) and cyclized (**11**) oligomers and polymers. To change the substituent effects of the monomer unit for the synthesis of polymers with a higher molecular weight and a ladder structure, we designed a 2,5-diaminoterephthalic acid-type monomer and study of its polymerization is in progress.

ACKNOWLEDGEMENTS

This work was partially supported by JSPS KAKENHI Grant Number 20550114.

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Supplementary Information accompanies the paper on Polymer Journal website (http://www.nature.com/pj)