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Synthesis of High Molecular Weight Poly(*p*-benzamide)s

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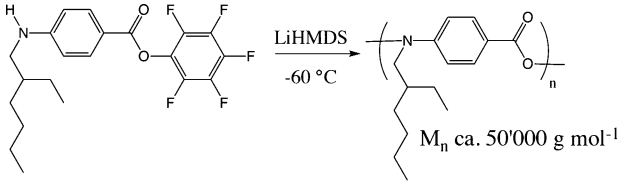
Supporting Information

ABSTRACT: The polymerization of aromatic para-amino acid ester derivatives was studied using model compounds. Mechanistic and kinetic experiments led to the discovery of some side reactions. Finally, high molecular weight poly(*p*-benzamide)s were synthesized and characterized. The use of highly reactive pentafluorophenol ester lead to polymers up to molecular weights of around 50 000 Da. Poly(benzamides) carrying both *N*-alkyl or *N*-benzyl groups on the amine could be polymerized to high molecular weight.



INTRODUCTION

Over the past decade, many efforts have been made to synthesize high molecular weight aromatic polyamides (aramides). The stability across a wide range of temperatures and the high tensile strength of such polymers make them interesting for the conception of high-tech materials. Kwolek at DuPont first reported the synthesis of aramide fibers using terephthaloyl chloride and phenylenediamine (AA- + BB-type monomers).[1−3] However, this methodology is only of limited use for the polymerization of amino acid (AB-type) monomers as they can only be converted into ammonium salts/acid chlorides under harsh conditions.[4] For the synthesis of high molecular weight polymers from amino acid monomers several alternative polymerization methods have been reported. Yamazaki et al. showed the direct polycondensation of *p*-aminobenzoic acid activating the carboxylic acid with triaryl phosphite and a tertiary amine like pyridine.[5−7] Similarly, Ogata and co-workers synthesized polyaramides activating the acid moiety using triarylphosophine, a polyhalo compound and a tertiary amine.[8−12] In both cases, polyaramides of molecular weights up to 10 000 Da were obtained.

More recently, Yokozawa and co-workers developed a polycondensation method that lead to polymers with narrowly distributed molecular weights following a chain-growth mechanism.[13] The polydispersity index of those polymers was comparable to those of polymers obtained by so-called living polymerizations. In their methodology, an *N*-silylated phenyl 4-(octylamino)benzoate was reacted with a fluoride source in order to create a highly reactive secondary anilide anion. Furthermore, this charge also induced a strong deactivating effect on the ester in para position, rendering the carbonyl group less electrophilic. Such monomers are therefore not able to react with themselves. The polymerization process is initiated with the addition of a highly electrophilic phenyl 4-nitrobenzoate ester. However, only polyaramides up to 24 000 Da were reported for this living polymerization.[14] Alternatively, the anilide anion could also be prepared from the aminoester monomer using strong non-nucleophilic bases such as lithium hexamethyldisilazide (LiHMDS).[15,16] The polymerization of phenyl *N*-alkyl or *N*-benzyl 4-aminobenzoate derivatives also lead to narrowly distributed polymers[17] and macrocycles.[18,19]

We recently reported the polymerization of trimers of derivatives of 4-aminobenzoic acid using Yokozawa's polymerization method in a step-growth polymerization context.[20,21] However, we were not able to synthesize high molecular weight polymers.

In order to synthesize high molecular weight polyamides using Yokozawa's polymerization method in a step-growth context, a better understanding of the side reactions occurring is required. Herein we report our investigations of side reactions as well as the synthesis of high molecular weight polyaramides up to M_n = 50 000 g mol^{-1} following a modification of the procedure reported by Yokozawa et al.[22] The polymers obtained are to the best of our knowledge the highest molecular weight A/B type aramide polymers to date.

EXPERIMENTAL SECTION

Materials and Instrumentation. Standard ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance spectra were recorded either on a Bruker Avance III 300 at a frequency of 300 and 75 MHz or at 400 MHz (^{1}H), 100 MHz (^{13}C), and 376 MHz (^{19}F) on a Bruker DPX 400 spectrometer. Transamidation studies were recorded at 500 MHz (^{1}H) on a Bruker Avance III (500 MHz) FT NMR spectrometer. All NMR signals were referenced internally to residual solvent signals. Matrix assisted laser desorption and ionization (MALDI) mass spectra were recorded on a Bruker ultrafleXtreme and electrospray ionization (ESI) mass spectra on a Bruker-Ion Trap MS esquire HCT mass spectrometer. For gel permeation chromatography in chloroform an instrument consisting of a Duratec vacuum degasser, a JASCO PU-2087plus pump and a set of two MZ-Gel SDplus linear columns (300 × 8 mm, 5 μm particle size) was used. Signal detection occurred by use of an Applied Biosystems 759A UV detector (set to 254 nm wavelength) and a Knauer Smartline 2300 RI-detector (refractive index). Calibration was done using Malvern PolycalTM UCS-PS polystyrene standards as for gel permeation chromatography in THF. The instrument is an automated Viscotek GPCmax VE-2001 with a set

of two Viscotek T6000 M linear columns (300 × 8 mm, 5 μm particle size). Signal detection occurred by use of an Viscotek Smartline 2600 UV detector (set to 254 nm wavelength) and a Vicotek VE 3580 RI-detector (refractive index).

Solvents of analytical grade were purchased from Honeywell, Acros Organics, Sigma-Aldrich, Fisher Scientific, and Fluka and were used without further purification. Solvents of technical grade were purified by distillation, if necessary. THF (extra dry) was purchased from Sigma-Aldrich. Deuterated solvents ($CDCl_3$, DMSO-d_6, THF-d_8) were purchased from Cambridge Isotope Laboratories, Inc. or ARMAR AG. Potassium peroxodisulfate was obtained from Merck and sodium triacetoxyborohydride from FluoroChem. All further chemicals were purchased from Sigma-Aldrich, Acros Organics or Alfa Aesar and used as received.

*2,5-Dihydroxy-4-nitrobenzoic Acid (**1**).*[23] 2-Hydroxy-4-nitrobenzoic acid (25 g, 137 mmol) was dissolved in a sodium hydroxide solution (500 mL, 2 M). Potassium peroxodisulfate in water (500 mL, 0.2 M) was added dropwise over 8 h. The solution was stirred for 7 days at room temperature. Potassium peroxodisulfate was added until HPLC showed total reaction of reactant. The solution was heated at 40 °C for 6 h before it was filtered. The pH was brought to 1 (some product already precipitated). The solution was heated at reflux for 48 h and cooled to room temperature. The pH was raised to 5 to 7 and the product precipitated. It was filtered and dried under vacuum to give **1** as a brown solid (10.61 g, 53.3 mmol, 39%). ^{1}H NMR (300 MHz, DMSO-d_6), δ, ppm: 7.91 (s, 1 H) 7.37 (s, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6), δ, ppm: 169.61 (1 Cq), 155.88 (1 Cq), 146.82 (1 Cq), 136.41 (1 Cq), 125.05 (1 Ct), 116.82 (1 Cq), 111.79 (1 Ct).

*Methyl 2,5-Dihydroxy-4-nitrobenzoate (**2**).* 2,5-Dihydroxy-4-nitrobenzoic acid (**1**) (0.17 g, 0.854 mmol) was dissolved in MeOH (3 mL, 0.28 M) in the presence of sulfuric acid (0.046 mL, 0.854 mmol). The solution was heated at reflux for 4 to 5 h, cooled down and poured into ice cold water. The product was filtered and dried under vacuum to give **2** as an orange solid (0.11 g, 0.516 mmol, 60%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 4.02 (s, 3 H) 7.68 (d, J = 4.9 Hz, 2 H) 9.76 (s, 1 H) 10.17 (s, 1 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 53.66 (1 Cp), 112.79 (1 Ct), 120.73 (1 Cq), 121.40 (1 Ct), 137.55 (Cq), 146.68 (1 Cq), 153.46 (1 Cq), 168.93 (1 Cq).

*Methyl 2,5-Bis((2-ethylhexyl)oxy)-4-nitrobenzoate (**3**).* Methyl 2,5-dihydroxy-4-nitrobenzoate (**2**) (1.75 g, 8.21 mmol) was dissolved with dry potassium carbonate (6.81 g, 49.3 mmol) in DMF (50 mL, 0.3 M) (the orange solid turned violet upon addition). 2-Ethylhexyl bromide (3.00 mL, 17.24 mmol) was added under a gentle flow of argon before the solution was heated at reflux for 48 h. The solution was poured into ice cold water and was left for precipitation overnight. The product was recovered by filtration and dissolved in DCM. The solution was dried over anhydrous magnesium sulfate. The solvent was removed and the compound dried under vacuum to give **3** as a light-yellow oil (2.11 g, 4.82 mmol, 59%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 0.83−0.99 (m, 12 H) 1.23−1.64 (m, 18 H) 1.66−1.86 (m, 2 H) 3.33−4.43 (m, 7 H) 7.41 (s, 1 H) 7.44−7.52 (m, 1 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 11.49 (2 Cp), 14.46 (2Cp), 23.39 (2 Cs), 24.13 (Cs), 29.40 (2 Cs), 30.74 (2 Cs), 39.75 (2 Ct), 52.92 (1Cp), 72.61 (1 Cs), 73.06 (1 Cs), 110.49 (1 Ct), 118.21 (1 Ct), 124.14 (1 Cq), 141.55 (1 Cq), 146.21 (1 Cq), 150.92 (1 Cq), 167.51 (1 Cq).

*2,5-Bis((2-ethylhexyl)oxy)-4-nitrobenzoic Acid (**4**).* Methyl-2,5-bis((2-ethylhexyl)oxy)-4-nitrobenzoate (**3**) (2.04 g, 2.66 mmol) was dissolved in a methanol/water mixture (10:1, 23 mL, 0.3 M) in the presence of sodium hydroxide (0.373 g, 9.32 mmol). The solution was heated at reflux for 14 h and cooled down. Methanol was removed under vacuum, and water was added. The solution was acidified to around pH = 7. The precipitated product was filtered, washed with cold water and dried under vacuum to obtain **4** as a dark red oil (1.86 g, 4.39 mmol, 91%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 0.78−1.05 (m, 12 H) 1.21−1.60 (m, 18 H) 1.66−2.00 (m, 2 H) 3.44−4.30 (m, 4 H) 7.52 (s, 1 H) 7.91 (s, 1 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 11.44 (2 Cp), 14.39 (2 Cp), 23.30 (2 Cs), 24.17 (2 Cs), 29.32 (2 Cs), 30.73 (2 Cs), 39.63 (2 Ct), 73.14 (1 Cs), 74.22 (1 Cs), 110.38 (1Ct), 119.79 (1 Ct), 122.31 (1 Cq), 141.72 (1 Cq), 147.44 (1 Cq), 150.71 (1 Cq), 164.06 (1 Cq).

*4-Amino-2,5-bis((2-ethylhexyl)oxy)benzoic Acid (**5**).* 2,5-Bis((2-ethylhexyl)oxy)-4-nitrobenzoic acid (**4**) (3.3 g, 7.79 mmol) was dissolved in ethyl acetate (60 mL, 0.13 M) and cooled to 0 °C. Palladium on charcoal (10%, 0.166 g, 0.156 mmol) was added to the tube, which was heated at 40 °C under an H_2 atmosphere of 35 bar for 72 h. The suspension was filtrated. The solvent was removed and the product was purified by column chromatography using ethyl acetate/hexane (1:4) as eluent to obtain **5** as a dark yellow oil (2.94 g, 7.47 mmol, 96%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 0.77−1.03 (m, 12 H) 1.20−1.58 (m, 17 H) 1.68−1.86 (m, 2 H) 3.75−4.09 (m, 3 H) 4.40 (br. s., 2 H) 6.33 (s, 1 H) 7.50 (s, 1 H) 10.87 (br. s. One H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 10.63 (2 Cp), 13.58 (2 Cp), 22.51 (2 Cs), 23.52 (2 Cs), 28.55 (2 Cs), 30.11 (2 Cs), 38.91 (2 Ct), 70.85 (1 Cs), 72.27 (1 Cs), 97.35 (1 Ct), 105.19 (1 Cq), 113.89 (1 Ct), 140.54 (1 Cq), 142.67 (1 Cq), 153.38 (1 Cq), 165.71 (1 Cq).

*Phenyl 4-Amino-2,5-bis((2-ethylhexyl)oxy)benzoate (**6**).* 4-Amino-2,5-bis((2-ethylhexyl)oxy)benzoic acid (**5**) (2.25g, 5.72 mmol) and phenol (0.807 g, 8.58 mmol) were mixed with phosphorus pentoxide (0.811 g, 5.72 mmol) and heated at 100 °C for 3 h. The mixture was then dissolved in DCM and filtered through Celite. The solution was washed with water, dried over magnesium sulfate and the solvent was removed under reduced pressure. The product was purified by column chromatography using ethyl acetate/hexane (1:8) as eluent to give **6** (1.12 g, 2.385 mmol, 42%). ^{1}H NMR (360 MHz, chloroform-*d*), δ, ppm: 0.73−1.04 (m, 12 H) 1.17−1.55 (m, 18 H) 1.71 (td, J = 11.3, 5.9 Hz, 2 H) 3.67−3.93 (m, 4 H) 6.24 (dd, J = 8.7, 2.6 Hz, 2 H) 6.35 (d, J = 2.7 Hz, 2 H) 6.69 (d, J = 8.9 Hz, 2 H). ^{13}C NMR (91 MHz, chloroform-*d*), δ, ppm: 11.47 (2 Cp), 14.43 (2 Cp), 23.40 (2 Cs), 24.27 (2 Cs), 29.43 (2 Cs), 30.92 (2 Cs), 39.83 (2 Ct), 71.21 (1 Cq), 71.67 (1 Cq), 103.14 (1 Ct), 112.60 (1 Ct), 137.62 (1 Cq), 141.59 (1 Cq), 154.37 (1 Cq).

*Phenyl 4-((2,4-Dimethoxybenzyl)amino)-2,5-bis((2-ethylhexyl)oxy)benzoate (**M1**).* Phenyl 4-amino-2,5-bis((2-ethylhexyl)oxy)-benzoate (**6**) (0.2 g, 0.426 mmol) was dissolved with 2,4-dimethoxybenzaldehyde (0.071 g, 0.426 mmol) in toluene (1 mL, 0.426 M) and refluxed under Dean−Stark conditions for 48 h. The solution was cooled to room temperature and the solvent evaporated. The formed imine was dissolved in dry methanol and dry THF (7 mL + 7 mL, 0.05 M) under an argon atmosphere and cooled to 0 °C. Sodium borohydride (0.019 g, 0.511 mmol) was added. The mixture was warmed to room temperature and stirred overnight. Water was added to the solution which was then extracted with DCM. The organic phase was washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed and the product was purified by column chromatography using ethyl acetate/hexane (1:8) as eluent to give **M1** (0.24 g, 0.387 mmol, 91%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 0.69−0.91 (m, 12 H) 1.09−1.48 (m, 18 H) 1.58 (d, J = 6.2 Hz, 2 H) 3.57−3.75 (m, 10 H) 4.16 (s, 2 H) 5.96−6.06 (m, 1 H) 6.19 (d, J = 2.8 Hz, 1 H) 6.24−6.40 (m, 4 H) 6.53 (d, J = 8.5 Hz, 1 H) 7.06 (dd, J = 13.6, 8.3 Hz, 2 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 11.39 (2 Cp), 14.34 (2 Cp), 23.33 (2 Cs), 24.21 (2 Cs), 29.36 (2 Cs), 30.88 (2 Cs), 39.76 (2 Cp), 42.86 (2 Cs), 55.08−56.03 (2 Cp), 61.57 (1 Cs), 71.01 (1 Cs), 71.52 (1 Cs), 98.71 (2 Ct), 99.26 (1 Ct), 99.95 (1 Ct), 104.03 (2 Ct), 111.30 (1 Ct), 120.17 (1 Cq), 122.11 (1 Cq), 129.61 (1 Ct), 129.82 (1 Ct), 139.93 (1 Cq), 141.27 (1 Cq), 154.76 (1 Cq), 158.62 (1 Cq), 158.73 (1 Cq), 160.31 (1 Cq), 160.86 (1 Cq).

Synthesis of Monomers M6 to M9. *2-((2-Ethylhexyl)oxy)-4-(isopropylamino)benzoic Acid (**12**).* 2-(2-Ethylhexyloxy)-4-amino benzoic acid (**9**) (560 mg, 2.11 mmol) was dissolved in DCM (2 mL), acetone (3 mL) and acetic acid (2 mL, 0.3 M) and stirred 5 min before addition of sodium triacetoxyborohydride (895 mg, 4.22 mmol). The solution was stirred for 48 h and quenched with sodium hydrogen carbonate solution. The organic layer was separated, dried over magnesium sulfate and the solvent was removed. The crude product was purified using column chromatography with ethyl acetate/hexane (1:3) as eluent to give **12** as a viscous colorless oil (180 mg, 0.585 mmol, 28%). ^{1}H NMR (400 MHz, chloroform-*d*), δ,

ppm: 0.69−1.10 (m, 6 H) 1.16−1.63 (m, 14 H) 1.82 (s, 1 H) 3.58−3.82 (m, 1 H) 4.06 (d, *J* = 5.4 Hz, 2 H) 6.09 (d, *J* = 2.1 Hz, 1 H) 6.25 (dd, *J* = 8.8, 2.1 Hz, 1 H) 7.95 (d, *J* = 8.7 Hz, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 11.03 (1 Cp), 13.96 (1 Cp), 22.72 (2 Cp), 22.79 (1 Cs), 23.78 (1 Cs), 28.73 (1 Cs), 30.35 (1 Cs), 39.23 (1 Ct), 44.08 (1 Ct), 71.20 (1 Cs), 95.15 (1 Ct), 105.09 (1 Cq), 106.23 (1 Ct), 135.31 (1 Ct), 152.65 (1 Cq), 159.51 (1 Cq), 166.09 (1 Cq).

*4-(Allylamino)-2-((2-ethylhexyl)oxy)benzoic Acid (**13**).* Allyl bromide (0.326 mL, 3.77 mmol) was added dropwise to a stirring solution of 4-amino-2-((2-ethylhexyl)oxy)benzoic acid (**9**) (1 g, 3.77 mmol) in DCM (7.54 mL, 0.5 M) with DIPEA (1 mL, 5.73 mmol) at 0 °C. The reaction was stirred for 4 h at 0 °C and allowed to stir overnight at room temperature. The solution was poured into water and filtered. The product was purified by column chromatography using ethyl acetate/hexane (1:3) as eluent to obtain product **13** (380 mg, 1.24 mmol, 33%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.78−1.05 (m, 6 H) 1.21−1.58 (m, 8 H) 1.76−1.89 (m, 1 H) 3.85 (br. s., 2 H) 4.07 (d, *J* = 5.4 Hz, 2 H) 4.59 (br. s., 1 H) 5.22 (d, *J* = 10.3 Hz, 1 H) 5.30 (d, *J* = 17.2 Hz, 1 H) 5.82−6.01 (m, 1 H) 6.15 (d, *J* = 1.8 Hz, 1 H) 6.30 (dd, *J* = 8.7, 1.9 Hz, 1 H) 7.95 (d, *J* = 8.7 Hz, 1 H) 10.68 (br. s., 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 11.01 (1 Cp), 13.95 (1 Cp), 22.57 (1 Cs), 23.42 (1 Cs), 28.53 (1 Cs), 29.92 (1 Cs), 39.18 (1 Ct), 45.32 (1 Cs), 71.03 (1 Cs), 95.12 (1 Ct), 105.79 (1 Cq), 106.37 (1 Ct), 116.44 (1 Cs), 133.94 (1 Ct), 135.12 (1 Ct), 153.35 (1 Cq), 159.13 (1 Cq), 165.42 (1 Cq).

*4-((2,4-Dimethoxybenzyl)amino)-2-((2-ethylhexyl)oxy)benzoic Acid (**14**).* 4-Amino-2-((2-ethylhexyl)oxy)benzoic acid (**9**) (1 g, 3.77 mmol) and 2,4-dimethoxybenzaldehyde (0.689 g, 4.15 mmol) were dissolved in DCM (6.28 mL, 0.5 M) and acetic acid (1.25 mL) and stirred for 1 h at room temperature. Sodium triacetoxyborohydride (1.597 g, 7.54 mmol) was added and the solution stirred for 24 h. The reaction was quenched with a saturated solution of sodium hydrogen carbonate. The organic layer was separated, dried over magnesium sulfate and the solvent was removed. The product was purified using a short silica column using ethyl acetate/hexane (1:3) as eluent to give **14** (1.52 g, 3.66 mmol, 97%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.79−1.04 (m, 6 H) 1.22−1.60 (m, 8 H) 1.69−1.91 (m, 1 H) 3.74−3.83 (m, 3 H) 3.85 (s, 3 H) 4.05 (d, *J* = 5.5 Hz, 2 H) 4.32 (s, 2 H) 6.17 (d, *J* = 2.1 Hz, 1 H) 6.33 (dd, *J* = 8.8, 2.1 Hz, 1 H) 6.46 (dd, *J* = 8.2, 2.4 Hz, 1 H) 6.50 (d, *J* = 2.3 Hz, 1 H) 7.17 (d, *J* = 8.3 Hz, 1 H) 7.94 (d, *J* = 8.7 Hz, 1 H) 9.13−11.54 (m, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 10.97 (1 Cp), 13.91 (1 Cp), 22.46 (1 Cs), 23.34 (1 Cs), 28.18 (1 Cs), 29.37 (1 Cs), 39.13 (1 Ct), 41.78 (1 Cs), 54.60 (2 Cp), 71.02 (1 Cs), 95.01 (1 Ct), 97.83 (1 Ct), 103.40 (1 Ct), 105.09 (1 Cq), 106.34 (1 Ct), 117.61 (1 Cq), 129.66 (1 Ct), 135.02 (1 Ct), 153.39 (1 Cq), 157.87 (1 Cq), 159.21 (1 Cq), 160.25 (1 Cq), 165.32 (1 Cq).

*General Procedure for the Synthesis of the Pentafluorophenyl Esters **M6** to **M9**.* The acid (1 equiv) was dissolved in DCM (0.5 M) in the presence of DMAP (0.2 equiv) and pentafluorophenol (1.5 equiv) and cooled to 0 °C. DCC (1.1 equiv) was added and the solution was stirred for 5 min. The solution was then allowed to warm to room temperature and stirred overnight. The suspension was filtered, the solvent was removed, and the crude product was purified via column chromatography using ethyl acetate/hexane (1:3) as eluent.

*Perfluorophenyl 4-Amino-2-((2-ethylhexyl)oxy)benzoate (**M6**).* 4-Amino-2-((2-ethylhexyl)oxy)benzoic acid (**9**) (1 g, 3.77 mmol) gave **M6** as a transparent oil (390 mg, 0.904 mmol, 24%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.69−1.03 (m, 6 H) 1.20−1.66 (m, 8 H) 1.66−1.90 (m, 1 H) 3.76−4.03 (m, 2 H) 4.05−4.54 (m, 3 H) 6.22 (d, *J* = 2.1 Hz, 1 H) 6.27 (dd, *J* = 8.6, 2.2 Hz, 1 H) 7.93 (d, *J* = 8.6 Hz, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 10.97 (1 Cp), 13.95 (1 Cp), 22.51 (1 Cs), 23.27 (1 Cs), 28.61 (1 Cs), 30.0 (1 Cs), 39.30 (1 Ct), 70.27 (1 Cs), 97.84 (1 Ct), 104.53 (1 Cq), 106.40 (1 Ct), 135.45 (1 Ct), 136.17 (1 Cq), 137.34 (1 Cq), 138.67 (1 Cq), 139.74 (1 Cq), 142.49 (1 Cq), 153.24 (1 Cq), 160.62 (1 Cq), 163.07 (1 Cq).

*Perfluorophenyl 2-((2-Ethylhexyl)oxy)-4-(isopropylamino)-benzoate (**M7**).* 2-((2-Ethylhexyl)oxy)-4-(isopropylamino)benzoic acid (**12**) (360 mg, 1.171 mmol) gave **M7** as a slightly yellow oil (450 mg, 0.95 mmol, 81%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.76−1.08 (m, 6 H) 1.15−1.62 (m, 14 H) 1.76 (d, *J* = 6.1 Hz, 1 H) 3.63−3.84 (m, 1 H) 3.84−4.00 (m, 2 H) 4.16 (br. s., 1 H) 6.08 (d, *J* = 1.0 Hz, 1 H) 6.18 (dd, *J* = 8.8, 2.0 Hz, 1 H) 7.94 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 11.02 (1 Cp), 13.98 (1 Cp), 22.75 (2 Cp), 22.90 (1 Cs), 23.54 (1 Cs), 28.82 (1 Cs), 30.04 (1 Cs), 39.35 (1 Ct), 44.04 (1 Ct), 70.25 (1 Cs), 95.65 (1 Ct), 102.98 (1 Cq), 104.63 (1 Ct), 135.38 (1 Ct), 153.51 (1 Cq), 160.36 (1 Cq), 162.98 (1 Cq).

*Perfluorophenyl 4-(Allylamino)-2-((2-ethylhexyl)oxy)benzoate (**M8**).* 4-(Allylamino)-2-((2-ethylhexyl)oxy)benzoic acid (**13**) (380 mg, 1.244 mmol) gave **M8** as a transparent oil (370 mg, 0.785 mmol, 63%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.71−0.91 (m, 6 H) 1.13−1.54 (m, 8 H) 1.62−1.72 (m, 1 H) 3.66−3.94 (m, 4 H) 4.38 (t, *J* = 5.7 Hz, 1 H) 5.16 (dd, *J* = 10.3, 0.6 Hz, 1 H) 5.19−5.31 (m, 1 H) 5.75−5.95 (m, 1 H) 6.04 (d, *J* = 2.1 Hz, 1 H) 6.13 (dd, *J* = 8.7, 2.0 Hz, 1 H) 7.85 (d, *J* = 8.8 Hz, 1 H).

*Perfluorophenyl 4-((2,4-Dimethoxybenzyl)amino)-2-((2-ethylhexyl)oxy)benzoate (**M9**).* 4-((2,4-Dimethoxybenzyl)amino)-2-((2-ethylhexyl)oxy)benzoic acid (**14**) (1.52 g, 3.66 mmol) gave **M9** as a transparent oil (1.15 g, 1.977 mmol, 54%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.76−1.09 (m, 6 H) 1.22−1.65 (m, 8 H) 1.77 (d, *J* = 6.0 Hz, 1 H) 3.79−3.85 (m, 4 H) 3.85−3.89 (m, 3 H) 3.89−3.97 (m, 2 H) 4.36 (d, *J* = 5.6 Hz, 2 H) 4.82 (s, 1 H) 6.19 (s, 1 H) 6.26 (dd, *J* = 8.8, 1.7 Hz, 1 H) 6.48 (dd, *J* = 8.6, 2.0 Hz, 1 H) 6.52 (d, *J* = 2.2 Hz, 1 H) 7.19 (d, *J* = 8.2 Hz, 1 H) 7.95 (d, *J* = 8.8 Hz, 1 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 11.02 (1 Cp), 13.69 (1 Cp), 22.75 (1 Cs), 23.46 (1 Cs), 28.65 (1 Cs), 30.06 (1 Cs), 39.32 (1 Ct), 42.05 (1 Cs), 54.93 (2 Cp), 70.41 (1 Cs), 95.60 (1 Ct), 98.76 (1 Ct), 103.42 (1 Cq), 104.04 (1 Ct), 104.73 (1 Ct), 118.16 (1 Cq), 129.79 (1 Ct), 135.20 (1 Ct), 154.48 (1 Cq), 158.35 (1 Cq), 160.50 (1 Cq), 160.73 (1 Cq), 163.06 (1 Cq). ^{19}F NMR (377 MHz, chloroform-*d*), *δ*, ppm: −163.81 to −162.81 (m, 2 F), −160.28 to −159.28 (m, 1 F), −152.70 (d, *J* = 17.7 Hz, 2 F).

*Perfluorophenyl 4-((2-Ethylhexyl)amino)benzoate (**M10**).* DCC (300 mg, 1.456 mmol) was added to a stirring solution of 4-((2-ethylhexyl)amino)benzoic acid (**11**) (330 mg, 1.323 mmol) with DMAP (32 mg, 265 *μ*mol) and pentafluorophenol (365 mg, 1.985 mmol) in dry DCM (2.2 mL, 0.6 M) at 0 °C. The solution was stirred for 5 min at 0 °C and then allow to stir a further 3 h at room temperature. The suspension was filtered and the solvent removed under reduced pressure. The residue was dissolved in DCM and washed with 0,5 M HCl and saturated sodium bicarbonate solution. The organic phase was dried over magnesium sulfate and the solvent was removed. The product was purified by column chromatography using ethyl acetate/hexane (1:20) as eluent to obtain product **M10** as a transparent oil (0.456 g, 1.09 mmol, 83%).^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 0.75−1.13 (m, 6 H) 1.21−1.54 (m, 8 H) 1.54−1.75 (m, 1 H) 3.14 (t, *J* = 5.9 Hz, 2 H) 4.18−4.77 (m, 1 H) 6.34−6.92 (m, 2 H) 7.76−8.32 (m, 2 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 10.76 (1 Cp), 13.95 (1 Cp), 22.16 (1 Cs), 23.72 (1 Cs), 27.91 (1 Cs), 29.46 (1 Cs), 38.99 (1 Ct), 43.93 (1 Cs), 111.45 (2 Ct), 112.22 (1 Cq), 132.97 (2 Ct), 136.25 (1 Cq), 137.49 (1 Cq), 138.70 (1 Cq), 139.91 (1 Cq), 142.33 (1 Cq), 152.22 (1 Cq), 162.01 (1 Cq).

*Perfluorophenyl 4-((2,4-Dimethoxybenzyl)amino)benzoate (**M11**).*[24] Same procedure as for **M9**. 4-Aminobenzoic acid (1 g, 7.29 mmol) was converted into **M11** over two steps and was recrystallized from ethyl acetate to give colorless crystals (1.2 g, 2.65 mmol, 36%). ^{1}H NMR (400 MHz, chloroform-*d*), *δ*, ppm: 3.84 (dd, *J* = 17.4, 0.9 Hz, 6 H) 4.36 (s, 2 H) 4.77 (br. s., 1 H) 6.47 (dd, *J* = 8.2, 1.3 Hz, 1 H) 6.51 (d, *J* = 1.3 Hz, 1 H) 6.67 (d, *J* = 8.1 Hz, 2 H) 7.18 (d, *J* = 8.2 Hz, 1 H) 8.00 (d, 2 H). ^{13}C NMR (101 MHz, chloroform-*d*), *δ*, ppm: 40.94 (1 Cs), 55.40 (2 Cp), 98.78 (1 Ct), 104.01 (1 Ct), 111.91 (2 Ct), 113.27 (1 Cq), 117.31 (1 Cq), 129.62 (1 Ct), 132.98 (2 Ct), 152.27 (1 Cq), 157.61 (1 Cq), 159.87 (1 Cq), 162.38 (1 Cq).

N-(2,4-Dimethoxybenzyl)aniline (DMB-aniline). Aniline (1 mL, 10.97 mmol) with 2,4-dimethoxybenzaldehyde (1.824 g, 10.97 mmol) were dissolved in DCM (27.4 mL, 0.4 M) and acetic acid (3.14 mL, 55 mmol) and stirred for 1 h. $NaBH(CH_3COO)_3$ (4.65 g, 21.95 mmol)

was added and the solution stirred for further 12 h. The reaction was quenched with a saturated solution of sodium bicarbonate and the product extracted with DCM. The solution was dried over magnesium sulfate and the solvent was remove under reduced pressure. The product was purified by column chromatography using ethyl acetate/hexane (1:5) as eluent to obtain the product as a colorless solid (2.44 g, 10.03 mmol, 91%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 3.88 (s, 3 H) 3.93 (s, 3 H) 4.20 (br. s, 1 H) 4.40 (s, 2 H) 6.53−6.65 (m, 2 H) 6.75−6.90 (m, 3 H) 7.27−7.37 (m, 3 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 42.70 (1 Cs), 55.25 (2 Cp), 98.32 (1 Ct), 103.66 (1 Ct), 113.20 (2 Ct), 117.36 (1 Ct), 119.63 (1 Cq), 129.30 (2 Ct), 129.76 (1 Ct), 148.33 (1 Cq), 158.14 (1 Cq), 160.74 (1 Cq).

N-(4-Methoxybenzyl)aniline (PMB-aniline). Aniline (1 mL, 10.97 mmol) with 4-methoxybenzaldehyde (1.335 mL, 10.97 mmol) were dissolved in DCM (27.4 mL, 0.4 M) and acetic acid (3.14 mL, 55 mmol). $NaBH(CH_3COO)_3$ (4.65 g, 21.95 mmol) was added and the solution stirred for further 12 h. The reaction was quenched with a saturated solution of sodium bicarbonate and the product extracted with DCM. The solution was dried over magnesium sulfate and the solvent was removed under reduced pressure. The product was purified by column chromatography using ethyl acetate/hexane (1:5) as eluent to obtain the product as a yellow liquid (2.27 g, 10.64 mmol, 97%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 3.81 (s, 3 H) 4.20 (br. s, 1 H) 4.36 (s, 2 H) 6.69−6.81 (m, 2 H) 6.82−6.91 (m, 1 H) 6.97−7.06 (m, 2 H) 7.25−7.37 (m, 3 H) 7.41 (d, J = 8.6 Hz, 2 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 47.59 (1 Cs), 55.10 (1 Cp), 112.72 (2 Ct), 113.88 (2 Ct), 117.32 (1 Ct), 128.65 (2 Ct), 129.11 (2 Ct), 131.30 (1 Cq), 148.08 (1 Cq), 158.70 (1 Cq).

N-(2,4-Dimethoxybenzyl)-2-methoxyaniline (DMB-o-anisidine). 2-Methoxyaniline (9.16 mL, 81 mmol) with 2,4-dimethoxybenzaldehyde (13.49 g, 81 mmol) were dissolved in toluene (162 mL, 0.5 M) and refluxed under Dean−Stark conditions for 2 days until the amount of recovered water corresponded to the number of reactant equivalents (81 mmol, around 1.5 mL). The solvent was removed under reduced pressure. THF (40 mL) along with methanol (40 mL, 1 M) were added to the imine and cooled to 0 °C under an argon atmosphere. Sodium borohydride (4.61 g, 122 mmol) was added and the solution was allowed to warm to room temperature and stir overnight. The reaction was quenched using water and the product was extracted with DCM, washed with brine, and dried over magnesium sulfate, and the solvent was removed to obtain the product as a brownish solid (21.14 g, 77 mmol, 95%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 3.82−4.02 (m, 9 H) 4.40 (s, 2 H) 6.51−6.61 (m, 2 H) 6.72−6.82 (m, 2 H) 6.85−6.92 (m, 1 H) 6.92−7.00 (m, 1 H) 7.28−7.37 (m, 1 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 42.48 (1 Cs), 54.62−55.75 (3 Cp), 98.46 (1 Ct), 103.78 (1 Ct), 109.31 (1 Ct), 110.19 (1 Ct), 116.25 (1 Ct), 119.84 (1 Cq), 121.21 (1 Ct), 129.41 (1 Ct), 138.35 (1 Cq), 146.87 (1 Cq), 158.32 (1 Cq), 160.02 (1 Cq).

2-Methoxy-N-(4-methoxybenzyl)aniline (PMB-o-anisidine). Aniline (1 mL, 10.97 mmol) with 2,4-dimethoxybenzaldehyde (1.824 g, 10.97 mmol) were dissolved in DCM (27.4 mL, 0.4 M) and acetic acid (3.14 mL, 55 mmol) and stirred for 1 h. $NaBH(CH_3COO)_3$ (4.65 g, 21.95 mmol) was added and the solution was stirred for further 12 h. The reaction was quenched with a saturated solution of sodium bicarbonate and the product extracted with DCM. The solution was dried over magnesium sulfate, and the solvent was removed under reduced pressure. The product was purified by column chromatography using ethyl acetate/hexane (1:5) as eluent to obtain the product as a white solid (2.44 g, 10.03 mmol, 91%). ^{1}H NMR (300 MHz, chloroform-*d*), δ, ppm: 3.88 (s, 3 H) 3.93 (s, 3 H) 4.20 (br. s, 1 H) 4.40 (s, 2 H) 6.53−6.65 (m, 2 H) 6.75−6.90 (m, 3 H) 7.27−7.37 (m, 3 H). ^{13}C NMR (75 MHz, chloroform-*d*), δ, ppm: 42.70 (1 Cs), 55.25 (2 Cp), 98.32 (1 Ct), 103.66 (1 Ct), 113.20 (2 Ct), 117.36 (1 Ct), 119.63 (1 Cq), 129.30 (2 Ct), 129.76 (1 Ct), 148.33 (1 Cq), 158.14 (1 Cq), 160.74 (1 Cq).

RESULTS AND DISCUSSION

In order to investigate potential side reactions during the Yokozawa-type polycondensation of our previously reported oligomers, we designed a monomer (**M1**) exhibiting the important features of the oligomers reported earlier.[21] **M1** was synthesized in seven straightforward steps as shown in Figure 1.

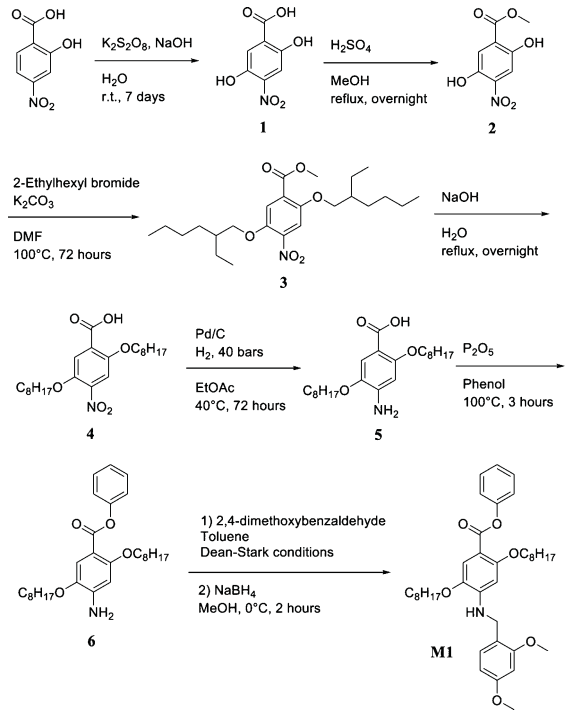


Figure 1. Synthetic pathway for the synthesis of monomer **M1**.

2-Hydroxy-4-nitrobenzoic acid was converted into 2,5-bishydroxy-4-nitrobenzoic acid (**1**, 39%) using Elbs persulfate oxidation.[23] A Fischer esterification gave the methyl ester (**2**, 60%) followed by a Williamson ether synthesis using 2-ethylhexyl bromide provided the highly organo soluble methyl 2,5-bis((2-ethylhexyl)oxy)-4-nitrobenzoate (**3**, 59%). Hydrolysis of the methyl ester gave the free acid (**4**, 91%) and the reduction of the nitro group under hydrogen pressure in the presence of palladium lead to the successful synthesis of the doubly substituted aromatic amino acid (**5**, 96%). Reaction with phenol and P_2O_5 gave the phenyl ester (**6**, 42%) followed by a reductive amination with 2,4-dimethoxy benzaldehyde to give monomer **M1** (91%).

Monomer **M1** carries two solubilizing alkyloxy side chains and a 2,4-dimethoxybenzyl amide *N*-protective group. The direct polymerization of primary amino acids such as phenyl 4-aminobenzoate following the procedure described by Yokozawa and co-workers is difficult to carry out as the secondary amide formed during the polymerization is more acidic than the primary amine of the monomer. Such an amide anion might be able to deactivate the ester in the para position, rendering it less electrophilic, and the solubility of the resulting polyanionic polyamide is expected to be low.[25] For this reason, all monomers used in this investigation were substituted by *N*-alkyl- or *N*-alkoxybenzyl protective groups.

We first polymerized **M1** (0.5 M) in dry THF using LiHMDS as the base and phenyl benzoate as the initiator varying the temperature from −20 °C to room temperature as well as the monomer to initiator ratio (see Table 1). The

resulting gel permeation chromatography (GPC in THF, against PS standards) elugrams all showed similar mass distributions and no control of the molecular weight.

Table 1. Results for the Polymerization of M1 at Different Temperatures or Amount of Initiator in THF

no.	T/°C	LiHMDS (equiv)	initiator (equiv)	M_n (g/mol)	M_w (g/mol)	Đ
1	r.t.	2	none	2900	4300	1.48
2	r.t.	2.2	0.01	1700	2300	1.32
3	−20	2.2	0.01	4800	6100	1.26
4	0	2	0.05	2600	4200	1.59

Neither the temperature nor the monomer to initiator ratio had any effect on the resulting molecular weights and lower temperatures led only to marginal improvements of the molecular weight distribution (Table 1, entry 3). However, matrix-assisted laser desorption ionization time-of-flight (MALDI-ToF) mass spectrometry showed additional mass distributions which could be assigned to polymers terminated with a benzamide group (see Supporting Information).

We attributed the latter to the substitution of the terminal phenyl ester with LiHMDS which results in a benzamide end group after aqueous work-up. Similar substitutions were already reported by Wannagat et al.[26] The MALDI-ToF mass spectra also showed the presence of several other mass distributions which could not be identified.

Model Reactions. In order to investigate the nucleophilic substitution of the phenyl ester during the polymerization we carried out a model reaction by adding either LiHMDS (Figure 2, bottom) or KHMDS (Figure 2, top) to phenyl benzoate

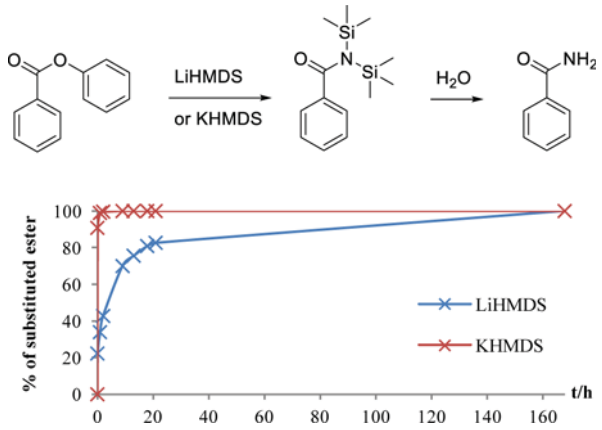


Figure 2. Model reaction carried out in THF-d_8 at room temperature and followed by ^{1}H NMR spectroscopy. Top: reaction scheme showing the substitution of phenyl benzoate with LiHMDS or KHMDS and their hydrolysis product, benzamide, after work-up. Bottom: Percentage of phenyl benzoate consumed over time (^{1}H NMR integration).

(0.12 M) at room temperature in THF-d_8 and followed the reaction over time by ^{1}H NMR spectroscopy. Room temperature was chosen for all side reactions investigated so that potential side products would form in higher quantities suitable for characterization by NMR.

In both cases the formation of phenol and *N*,*N*-bis-(trimethylsilyl)benzamide could be observed after several minutes. Furthermore, integration of the side product signals of the ^{1}H NMR spectrum allowed us to plot the product formation over time (see Supporting Information). After 5 min. 22% of the initial phenyl benzoate had already reacted with LiHMDS whereas KHMDS had already substituted 91% of phenyl benzoate. The NMR-reaction products after aqueous work-up were analyzed using high pressure liquid chromatography (HPLC) comparing their retention times with that of pure phenol and benzamide, confirming our observation. This model experiment shows the strong effect of the counterion on the nucleophilicity of the reagent and indicates that lower temperatures will be necessary to suppress the nucleophilic attack of the base in order to obtain higher molecular weight polyamides.

In a second investigation, we wanted observe the stability of the *N*-benzyl protected aniline in the presence of strong bases. Four different model compounds were therefore prepared via reductive amination using the corresponding aromatic primary amines, the aldehyde along with sodium triacetoxyborohydride in an acetic acid and dichloromethane mixture (Figure 3).

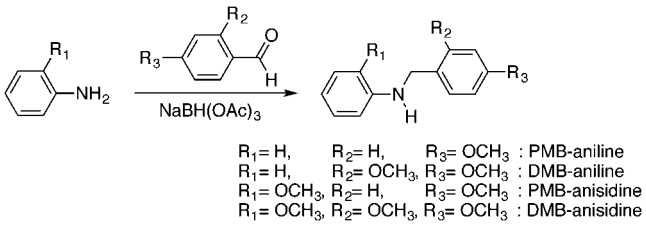


Figure 3. Synthesis of *N*-benzylamine model compounds.

^{1}H NMR spectra of *N*-(2,4-dimethoxybenzyl)aniline (DMB-aniline), *N*-(4-methoxybenzyl)aniline (PMB-aniline), *N*-(2,4-dimethoxybenzyl)-2-methoxyaniline (DMB-anisidine) and 2-methoxy-*N*-(4-methoxybenzyl)aniline (PMB-anisidine) were recorded in THF-d_8 in the presence of LiHMDS or KHMDS.

Surprisingly, the formation of stable side product could be observed in all cases which were identified as the corresponding imines (see Supporting Information). The benzyl protected anilide anion is partially converted into an imine most likely via a *β*-hydride elimination. ^{6}Li NMR did not prove this assumption, either due to the poor solubility of lithium hydride in THF or due to further reactions with protic impurities. The potential of LiHMDS as a hydride donor has been reported previously.[27−29]

However, only Wittig and co-workers described the formation of imines via *β*-hydride elimination in the presence of LiHMDS or LDA which may involve a single electron transfer (SET).[30−34] The identity of the imines could be confirmed by electrospray ionization mass spectrometry (see Supporting Information). The amount of imine formed with either lithium or potassium as counterion is reported in Table 2. The formation of the imine side product via hydride elimination of the anilide anion showed no dependence on the counterion.

The presence of one chelating ortho methoxy group appeared to favor imine formation (entries 3−5) but a detailed investigation into the substituent effects has not yet been carried out. Surprisingly, no presence of imine side products was observable in the presence of two ortho methoxy chelating groups (Table 2, entry 6). The same experiment repeated with *N*-(1-phenylethyl)aniline, *N*-(2-phenylpropan-2-yl)aniline or *N*-allylaniline as alternative amine protecting groups in the

Table 2. ^{1}H-NMR (THF-d_8) Experiment: *N*-Benzyl Protected Anilines Reacting with LiHMDS or KHMDS under Hydride Elimination Forming Imines

no.	reactant	base	amount of imine (%)
1	PMB-aniline	LiHMDS	9
2	PMB-aniline	KHMDS	7
3	DMB-aniline	LiHMDS	14
4	DMB-aniline	KHMDS	19
5	PMB-*o*-anisidine	LiHMDS	17
6	DMB-*o*-anisidine	LiHMDS	not observed

presence of LiHMDS did also not lead to imine side products (see Supporting Information).

The formation of imines under polymerization conditions will necessarily lead to premature termination of the polymerization and thereby limit the accessible molecular weight. Polymerizations at lower temperatures will likely slow down this side reaction.

The last side reaction investigated in our study was chain transfer to the polymer, i.e., the reaction of activated monomer with an amide group of the main chain rather than the ester at the chain end of the polymer. Such side-reactions would lead to broadening of the molecular weight distribution, lowering of the molecular weight and be indistinguishable in the final polymer product from self-initiated polymerizations. We therefore investigated the model reaction shown in Figure 4 (top) in an ^{1}H NMR-reaction (THF-d_8).

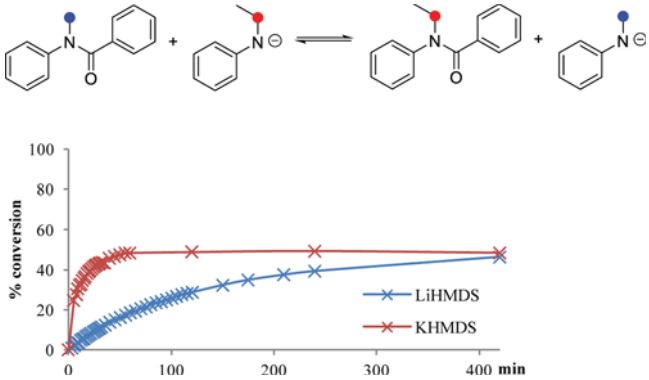


Figure 4. Model reaction carried out in THF-d_8 at room temperature and followed by ^{1}H NMR spectroscopy. Top: reaction scheme showing the equilibrium reaction between *N*-methylbenzanilide with lithium or potassium *N*-ethylanilide. Bottom: Conversion of the above reaction followed by ^{1}H NMR spectroscopy.

N-Ethylaniline (*N*-EtA) was either deprotonated with LiHMDS or KHMDS and served as the model for the activated monomer. *N*-methylbenzanilide (*N*-MeBA) which served as model for the polymer backbone amides was added to the *N*-EtA anion and the reaction was monitored over time by ^{1}H NMR spectroscopy at room temperature As shown in Figure 4 (bottom) a transamidation reaction occurs immediately and reaches an equilibrium at 50% conversion of *N*-EtBA (the ^{1}H NMR signals of the ethyl CH_2 of *N*-EtBA were compared to those of the CH_2 of the *N*-EtA anion, alternatively the CH_3 signals of *N*-MeA anion were compared to those of the *N*-MeBA product).

Equilibrium (50% conversion) was reached after ca. 7 h in the case of LiHMDS and already after 1 h for KHMDS. The trend observed earlier (Figure 2) that the larger potassium counterion increases the nucleophilicity of the reagent compared to lithium is observed for the amide formation as well.[35] Such transamidation reactions would clearly lead to a broadening of the dispersity of the final polyamide. We believe that this side reaction could also be avoided by reducing the reaction temperature. Figure 5 graphically summarizes all side reactions investigated in our study.

On the basis of our findings from model reactions we first investigated less reactive ethyl ester monomers (**M2**–**M5**, see Supporting Information). We believed that ethyl esters would not be rapidly substituted by the lithium base. However, the reactivity of the ethyl ester was too low even at 0 °C to allow the formation of higher molecular weight polymers. We therefore next explored another strategy using monomers carrying a highly reactive pentafluorophenyl (PFP) ester under polymerization temperatures below −50 °C.

In order to investigate the polymerization potential of a monomer carrying a PFP ester, we prepared six monomers (**M6**–**M11**, Figure 6). **M6**–**M9** were synthesized from the soluble aromatic amino acid **9**, a 4-aminosalicylic acid derivative (see Supporting Information). The two intermediates **12** and **14** were obtained after a reductive amination with sodium triacetoxyborohydride in acetic acid and dichloromethane using acetone (**12**, 28%) or 2,4-dimethoxybenzaldehyde (**14**, 97%) as the electrophiles. The allyl substituted reactant **13** was prepared by adding allyl bromide to the reactant **9** (33%). The PFP esters of compounds **9**, **12**, **13** and **14** were all prepared using Steglich esterifications to give monomers **M6** (24%), **M7** (81%), **M8** (63%), and **M9** (54%). **M10** was obtained after a reductive amination of 4-aminobenzoic acid with 2-ethylhexanal (**11**, 92%, supporting info) followed by a Steglich esterification (**M10**, 83%). Following the same procedure as for **M9**, 4-

Figure 5. General scheme for the polymerization of aromatic amino acid derivatives initiated by phenyl benzoate using lithium bis(trimethylsilyl)amide and the possible side reactions (R = $C_8H_9O_2$ or C_7H_{15} and R′ = ethyl, phenyl or pentafluorophenyl).

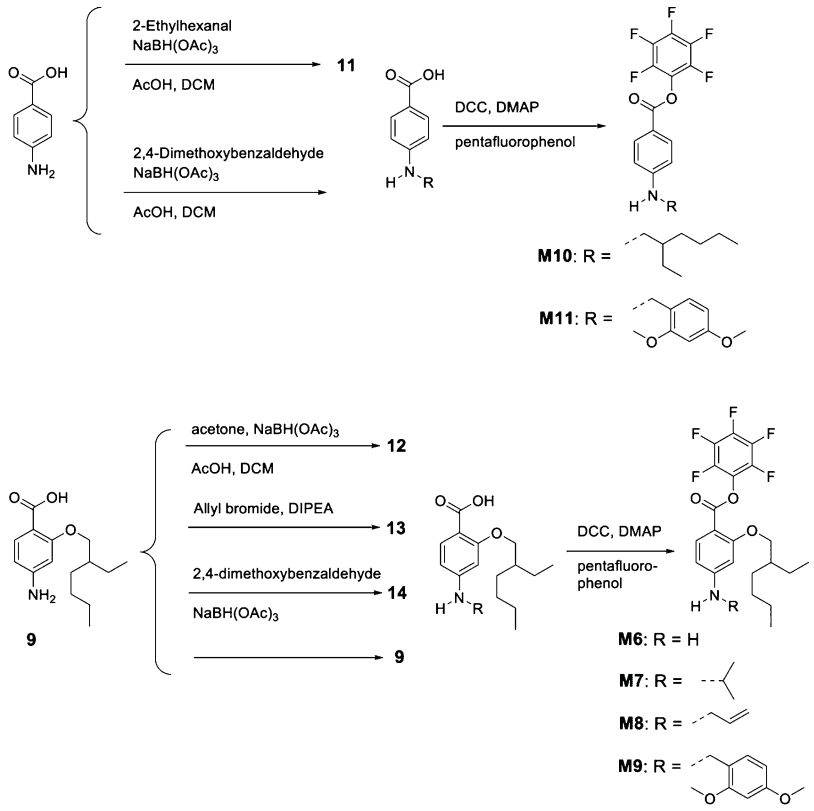


Figure 6. Synthesis of pentafluorophenyl ester monomers **M6**–**M11**.

Table 3. Results from the Polymerized PFP Ester Monomers M6–M10 Measured on a THF GPC (UV Signal)

no.	monomer	temperature (°C)	base (equiv)	initiator (equiv)	M_n (g/mol)	M_w (g/mol)	$Đ$
1	**M6**	−60	LiHMDS (2.1)	0.01	1900	2200	1.14
2	**M7**	−50	LiHMDS (1.1)	0.01	1800	2000	1.12
3	**M8**	−60	LiHMDS (3)	0.01	1700	1800	1.05
4	**M9**	−60	LiHMDS (1)	0.01	1850	2100	1.17
5	**M9**	−40	KHMDS (1)	0.01	1700	1950	1.14
6	**M10**	−60	LiHMDS (2)	0.01	26 800	43 500	1.62
7	**M10**	−60	LiHMDS (2)	0.0025	53 400	129 300	2.42
8	**M10**	−60	LiHMDS (4)	0.01	4800	7400	1.54

aminobenzoic acid was converted into **M11** (36% over two steps).[24]

Monomers **M6**–**M11** were all polymerized following the same procedure: the base (1 M in THF) was cooled to the desired temperature before addition of the initiator in THF (1 M). The monomer (1 M solution in THF) was then added dropwise to the cooled solution.

Table 3 shows that even using PFP esters all monomers carrying 2-(2-ethylhexyloxy) substituents did not polymerize to high molecular weights. This might be due to steric effects from the bulky alkyloxy side chain ortho to the activated ester but also a result of the reduced ester electrophilicity caused by this electron donating substituent. Further experiments carried out on **M9** raising either the temperature (−40 °C or −20 °C) or using a more electrophilic pentafluorophenyl benzoate initiator did not yield higher molecular weights.

Monomer **M10** which lacks the ortho alkoxy substituent, on the other hand, showed promising results, giving a polymer near the expected molecular weight (Table 3 entry 6, expected M_n = 25 000 Da, observed M_n = 26 000 Da, $Đ$ = 1.62).

A lower initiator loading of 0.0025 equiv yielded an even higher molecular weight polymer albeit less than what was expected (Table 3 entry 7, expected M_n = 100 000 Da, observed M_n = 53 000 Da, $Đ$ = 2.42). The molecular weight distributions for both samples indicated a nonliving character of the polymerization. The GPC elugrams indicated monomodal molecular weight distributions (see Figure 7 as an example).

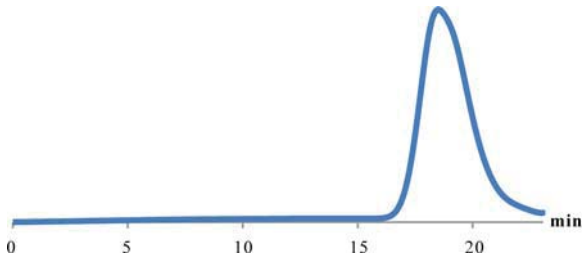


Figure 7. UV signal of the GPC chromatogram of poly(**M10**) of M_n 53 000 measured in THF.

Table 4. Results from the Polymerized PFP Ester Monomer M10 Measured on a THF GPC (UV Signal)

no.	LiTMP (equiv)	concentration	temperature (°C)	initiator (equiv)	M_n (g/mol)	M_w (g/mol)	$Đ$
1	1.5	1	−60	0.01	31 000	70 000	2.19
2	3	0.35	−60	0.01	12 700	21 800	1.72
3	3	0.35	−40	0.0025	11 700	17 300	1.48
4	1.5	0.35	−60	0.0025	35 000	180 000	5.14
5	1.5	0.35	−60	0	9 000	18 500	2.05
6	1.5	0.35	−60	0.01	15 800	33 100	2.09

Polymers from monomers **M8** and **M9** (Table 3, entry 3 and 4) were of low molecular weight and could therefore be investigated using MALDI-ToF MS to investigate their end-group composition. The main distribution of the mass spectra can be assigned to self-initiated polymers which carry benzamide end groups (see Supporting Information). This result shows clearly that even at temperatures as low as −60 °C, LiHMDS is able to substitute the terminal PFP ester, thereby stopping the polymerization. Compared to monomers **M6**−**M9**, **M10** is less sterically hindered, its phenyl ring is less electron rich and its amine more basic. It is therefore reasonable to assume that the propagation of **M10** is sufficiently fast to kinetically compete with the above side reaction of LiHMDS if the molecular weight aimed for is not too high (see Table 3 entry 6 vs entry 7).

Actually, **M6** to **M9** could be electronically disfavored due to the donating effect of the alkyl ether on position 2 to the PFP carbonyl, decreasing its electrophilicity. Moreover, the aniline substituent being only weak electro-donating groups, the nucleophilic character of the amine anion could be decreased, thus rendering such type of monomer not suitable for anionic polymerization. In order to prove this explanation, we polymerized perfluorophenyl 4-((2,4-dimethoxybenzyl)amino)-benzoate (**M11**, **M9** without alkyl ether substituent) at different temperature using phenyl benzoate as initiator. This monomer could be polymerized well even at −40 °C giving MW compounds of around 6000 Da with broad polydispersity when aiming 25 000 Da. The low polymerization degree was attributed to the low solubility of the polymers and the ester substitution with LiHMDS.

We attribute the broad polydispersities of all polymerizations in Table 3 to the ester substitution by LiHMDS. We therefore changed the base to lithium 2,2,6,6-tetramethylpiperidine (LiTMP) which is less nucleophilic than LiHMDS and has a pK_a = 37 which is higher than that of LiHMDS (pK_a = 30).[36,37] Because of the poor solubility of LiTMP in THF, the concentration of the solution had to be decreased to 0.35 M. Polymerizations at higher concentration gave polymers with bimodal distributions (Table 4, entry 1), which is most likely a consequence of initiation events at different times. As LiTMP is not stable enough to be stored, it was prepared in situ by the addition of *n*-butyllithium to 2,2,6,6-tetramethylpiperidine in THF before addition of the initiator and the monomer. As LiTMP is not nucleophilic, an excess of base should not influence the outcome of the polymerizations. In fact, the molecular weight of the polymers does not seem to change with increasing amounts of LiTMP (Table 4, entry 2 and 6).

Compared to polymerization with LiHMDS, the final polymer still carries the PFP ester at the chain end as was evident from its ^{19}F-NMR spectrum (see Supporting Information). Such monoend functional polymers could in principle be used for end-functionalization reactions or diblock copolymer formation.

We speculated that the LiTMP *N*-deprotonated monomer could still self-initiate the polymerization at −60 °C. This would explain the broad polydispersities observed in particular when low initiator concentrations were employed (Table 4, entry 4). Furthermore, this self-initiation appears more pronounced at higher temperatures decreasing the final molecular weight of the polymer (Table 4, entry 3 vs 4). To demonstrate that self-initiation is indeed a prominent side reaction, monomer **M10** was added to LiTMP in the absence of initiator. This gave a polymer of 9 000 g mol^{-1} (Table 4, entry 5), thus showing the high reactivity of PFP esters even at −60 °C. To show the influence of the initiator, the exact same conditions were employed but this time with initiator present (Table 4, entry 6). A polymer of slightly higher molecular weight (but similarly broad polydispersity) was obtained.

As the lithiated monomer is identical regardless of the base employed (LiHMDS or LiTMP) we concluded that the increased tendency for self-initiation in the case of LiTMP is a direct result of the slow deprotonation reaction using this base. To obtain further support for this hypothesis we next polymerized monomer **M11** in the presence of LiTMP. The dimethoxybenzyl *N*-protective group on **M11** is less bulky than the 2-ethylhexyl group on monomer **M10**. The deprotonation reaction between LiTMP and **M11** should therefore occur more rapidly leading to less self-initiation and hence higher molecular weights. The reaction of **M11** with LiTMP was carried out at −40 °C and the polymer obtained had a molecular weight close to the one aimed for (M_n = 44 000 g mol^{-1},$Đ$= 3.2; target M_n = 45 000 g mol^{-1}). Polymer like poly(**M11**) are interesting materials as the *N*-protective group can in principle be removed in postpolymerization reactions to liberate the unprotected polyaramid. The activated PFP ester end group could allow the conjugation with end-functional coil-like polymers. This might therefore be an attractive synthetic route for the synthesis of rod−coil block copolymers or other supramolecular polymeric architectures.

From these results, we propose that the most important side reaction when aiming for high molecular weight polyaramides via the activated monomer route is ester substitution by the nucleophilic base. Care therefore needs to be taken that a non-nucleophilic base is employed. However, sterically hindered bases might result in slow deprotonation reactions of the monomer thereby leading to increased self-initiation. In the case of monomer **M11**, a good compromise was found, but the polydispersity $Đ$ = 3.2 indicates that a significant amount of self-initiation was still present. The optimization of this reaction is currently being investigated and will be reported in due course.

CONCLUSIONS

Herein we demonstrate the polymerization of aromatic amino acid derivatives to very high molecular weight polyamides. We present several important side reactions that might be

operational during the polymerization reaction depending on monomer structure or the nature of the base employed.

Taking these side reactions into account we show that a successful synthesis of high molecular weight polyaramids can be achieved. The synthetic route described opens up a wide range of high molecular weight aramides some of which carry activated esters at their chain ends which are suitable for postpolymerization functionalization reactions. The anionic polymerization of highly electrophilic pentafluorophenol ester monomers was investigated using two different bases, LiHMDS and LiTMP. The former shows significant nucleophilic side reactions that ultimately limit the polymerization to molecular weights below 50 000 g mol^{-1}. The latter exhibits virtually no nucleophilicity but reacts very slowly in the deprotonation of the amino ester monomer thereby leading to an increase of self-initiated polymerization. One monomer (**M11**) was sterically less demanding and could be deprotonated faster even by the sterically demanding base LiTMP. This allowed the synthesis of polyaramids up to 44 000 g mol^{-1}.

■ ASSOCIATED CONTENT

Experimental procedures, ^{1}H and ^{13}C NMR spectra, MALDI-ToF mass spectrometric data(PDF)

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The authors declare no competing financial interest.

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