European Polymer Journal 45 (2009) 3210–3216

Contents lists available at ScienceDirect

European Polymer Journal

journal homepage: www.elsevier.com/locate/europolj

Solid phase synthesis of aromatic isophthalic oligoamides with controlled molecular weight

J.L. Santiago-Garcia, M. Aguilar-Vega *

Centro de Investigación Científica de Yucatán A.C. Unidad de Materiales, Calle 43 # 130, Col. Chuburná de Hidalgo, 97200 Mérida, Yucatán, México

ARTICLE INFO

Article history:
Received 10 March 2009
Received in revised form 24 July 2009
Accepted 27 July 2009
Available online 3 August 2009

Keywords:
Solid phase synthesis
Aromatic oligoamides
Polycondensation
Thermal properties

ABSTRACT

The synthesis of oligo(hexafluoroisopropylidene isophthalamide) on a solid support of SynPhase™ Lanters is described. The repetitive coupling steps using symmetrical diamines and diacid chlorides allows to obtain aromatic oligoamides with controlled molecular weight ($\overline{M}_w$ = 5480 g/mol) and narrow molecular weight distribution (PDI = 1.03) as evidenced by gel permeation chromatography. Moreover, the FTIR and ^{1}H NMR analysis demonstrated their chemical nature and OH-end groups functionality. The thermal properties of aromatic oligoamides were found to be lower, as expected, than those of poly(hexafluoro-isopropylidene isophthalamide), the same repeating unit high molecular weight polyamide, as judged by differential scanning calorimetry and thermogravimetrical analysis.

1. Introduction

Wholly aromatic polyamides (aramids) have received considerable attention with regard to the production of high-performance materials, due to their outstanding thermal stability, chemical resistance, low flammability, and mechanical properties [1]. However, the poor solubility and high softening temperature caused by the chain stiffness and their intermolecular hydrogen bonding lead to difficulties for processing of these materials. Breaking intermolecular hydrogen bonds is a typical approach to improve solubility and processability while maintaining the high thermal stability. Generally, it has been more convenient to synthesize modified aramids via the structural modification of diamine monomers, such as the incorporation of bulky pendant groups of hexafluoroisopropylidene (6F) [2], followed by the polycondensation reaction with available aromatic dicarboxylic acids [3] or their derivatives [1,4]. However, the materials synthesized by polycondensation present a broad molecular weight distribution, which in turn influences their physical properties often in uncontrolled ways [5]. Therefore, it is interesting to prepare aromatic oligoamides with a controlled degree of polymerization. The aromatic oligoamides will provide the opportunity to design and produce well-defined and characterized segments with some defined functionalities and properties. Therefore, the current challenge is to precisely control the structure, polydispersity, and dimensions of aromatic oligoamides, prepared by polycondensation, in such a way that specific properties or functionalities can be obtained and can be used to study the relationship between chain length and their ultimate physical and chemical properties.

Since 1963, the introduction of solid phase synthesis has been studied extensively for the synthesis of oligopeptides and oligonucleotides [6]. Recently, this synthetic technique has been employed in the preparation of well-defined polymers enabling the convergence between the synthetic organic and polymer chemistry [7–11]. Despite their importance, there are few reports describing the synthesis of aromatic polyamides on solid support, even though this method was widely use for polypeptides which are natural polyamides. König et al. [12] described a traditional solid supported synthesis of oligo(*p*-benzamide),

* Corresponding author. Tel.: +52 999 942 8330; fax: +52 999 981 3900.
E-mail addresses: mjav@cicy.mx, manualito@gmail.com (M. Aguilar-Vega).

0014-3057/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.eurpolymj.2009.07.020

using a Wang resin support and *p*-amino benzoic acid with carboxylic acids groups activated *in situ* with thionyl chloride, and amine groups protected with *p*-methoxy benzyl (PMB) and 9-fluorenylmetohoxycarbonyl (Fmoc). Nakata and Brisson [13] developed a quasi-Merrifield approach to synthesize monodisperse polyamide oligomers using bifunctional monomers avoiding the step of protection and deprotection. More recently, Hartmann et al. [14] using the solid phase synthesis, synthesized monodisperse sequence-defined poly(amidoamines) (PAA) segments. This synthesis includes the alternating addition of succinic acid and diamines. Traditionally, the Wang resin is without doubt the most widely used solid support in solid phase synthesis. In Wang resin the swelling factor is important since reaction kinetics is diffusion controlled. Consequently, resin that swells more will have a higher diffusion rate of reagents into the core of the matrix, resulting in shorter reaction times and more complete chemical conversions. This process is eliminated using SynPhase™ Lanterns supports which are open structural forms with a large surface area and functional groups in the surface that allow a direct reaction that is not controlled by swelling and diffusion inside the resin.

The main objective of this work is to evaluate the solid phase synthesis of aromatic oligoamides with controlled molecular weight. This proof of concept was carried out utilizing a solid support of SynPhase™ Lanterns hydroxymethylated, on which the stepwise growth of the aromatic oligoamide was carried out by alternating addition of 4,4′-hexafluoroisopropylidene diamine (HFA) and isophthaloyl chloride (ISO).

2. Experimental

2.1. Materials

The solid support SynPhase™ Lanterns hydroxymethylated were purchased from Mimotopes, Pty Ltd., Clayton, Australia. Isophthaloyl chloride (ISO) was distilled under vacuum prior to use. 4,4′-hexafluoroisopropylidene diamine (HFA). Triethylamine (TEA), dichloromethane (DCM) and *N*-methyl pyrrolydone (NMP) were stored over 4 Å molecular sieves. All reactants and solvents were purchased from Aldrich Chemical Co. and used as received unless otherwise stated.

2.2. Benzoylation of SynPhase™ Lanterns hydroxymethylated

Five independent hydroxylated supports (with a 15 μmol −OH groups each one for a total of 75 μmol of OH groups) were placed in a 50 mL flask equipped with inlet and outlet nitrogen. Next, a solution of 0.75 mmol of ISO and 1.5 mmol of TEA in 20 mL of DCM was added slowly at room temperature while stirring under nitrogen. The benzoylation reaction was carried out for 2 h. Then the ISO solution was drained and the SynPhase™ Lanterns were rinsed vigorously with 10 mL of DCM three times during 5 min to remove excess reagents and reaction byproducts, and dried under vacuum.

2.3. Synthesis of aromatic oligoamides

The first step to synthesize aromatic oligoamides was the benzoylation of SynPhase™ Lanterns described above using a 50 mL three-neck flask with bottom outlet. After the elimination of excess reagents, byproducts, and solvents; the sterificated SynPhase™ Lanterns supports were treated with a solution containing 0.25 g (0.75 mmol) of HFA and 0.21 mL (1.5 mmol) of TEA in 5 mL of NMP (Fig. 1 step 2). This solution was added with the help of a syringe while stirring under nitrogen atmosphere. The reaction proceeded during 2 h and then the excess reagents were drained and the supports were rinsed with NMP (3 min/3 times) and DCM (3 min/3 times). Subsequently, the SynPhase™ Lanterns supports were treated with 0.153 mg (0.75 mmol) of ISO and 0.21 mL (1.5 mmol) of TEA in 5 mL of DCM (Fig. 1 step 3). This solution was added with the help of a syringe while stirring under nitrogen atmosphere. The reaction proceeded during 2 h and then the excess reagents were drained and the supports were rinsed with DCM (3 min/5 times). All the rinses were carried out in nitrogen atmosphere. In step 4 (Fig. 1), the solutions containing the diamine or the dichloride were added alternatively until the degree polymerization desired ($n = 10$) was obtained. The aromatic oligoamides were separated of the solid support with a 33% hydrogen bromide in acetic acid solution (cleaving solution) during 1 h (Fig. 1 step 5). After, that time the solid supports and the cleaving solution were separated and dried under vacuum. Both fractions were extracted with NMP; these solutions were mixed and neutralized in methanol during 6 h. The aromatic oligoamides were isolated by pouring the methanolic mixture into 500 mL of distilled water.

2.4. Characterizations

The aromatic oligoamides were characterized using a Nicolet 460 FTIR spectrometer, the spectra were acquired with 4 cm^{-1} resolution at 100 scans in the absorption mode between 4000–400 cm^{-1}, utilizing KBr tablets with 2% (w/w) of aromatic oligoamides. The spectra were corrected for KBr background using the OMNIC software. The ^{1}H-NMR spectra was recorded on a Bruker Advance 400 spectrometer in DMF-d_7 with 4.5% (w/v) LiCl solution and TMS as internal standard, chemical shifts are recorded in ppm values. Gel permeation chromatography (GPC) analysis of the samples was performed on a HP Agilent 1100 HPLC system equipped with a differential refractive index detector. DMF with 4.5% (w/v) LiCl was used as the mobil phase at a flow rate of 1 mL/min. The sample concentration was 1 mg/mL and the injection volume was 20 μL. Calibration was accomplished with polystyrene (PS) standards (from Polymer Laboratories) and molecular weights ranged from 10^4 to 5.8×10^2. A Zorbax PSM 60-S 6.2 × 250 mm column was used for calibration and calculation. Differential scanning calorimetry (DSC) was performed in a differential scanning calorimeter DSC-7 Perkin-Elmer. Experiments were performed on 7.5 mg samples at a heating rate of 10 °C/min over the temperature range of 50–300 °C under nitrogen atmosphere. Thermogravimetric analysis was performed on a

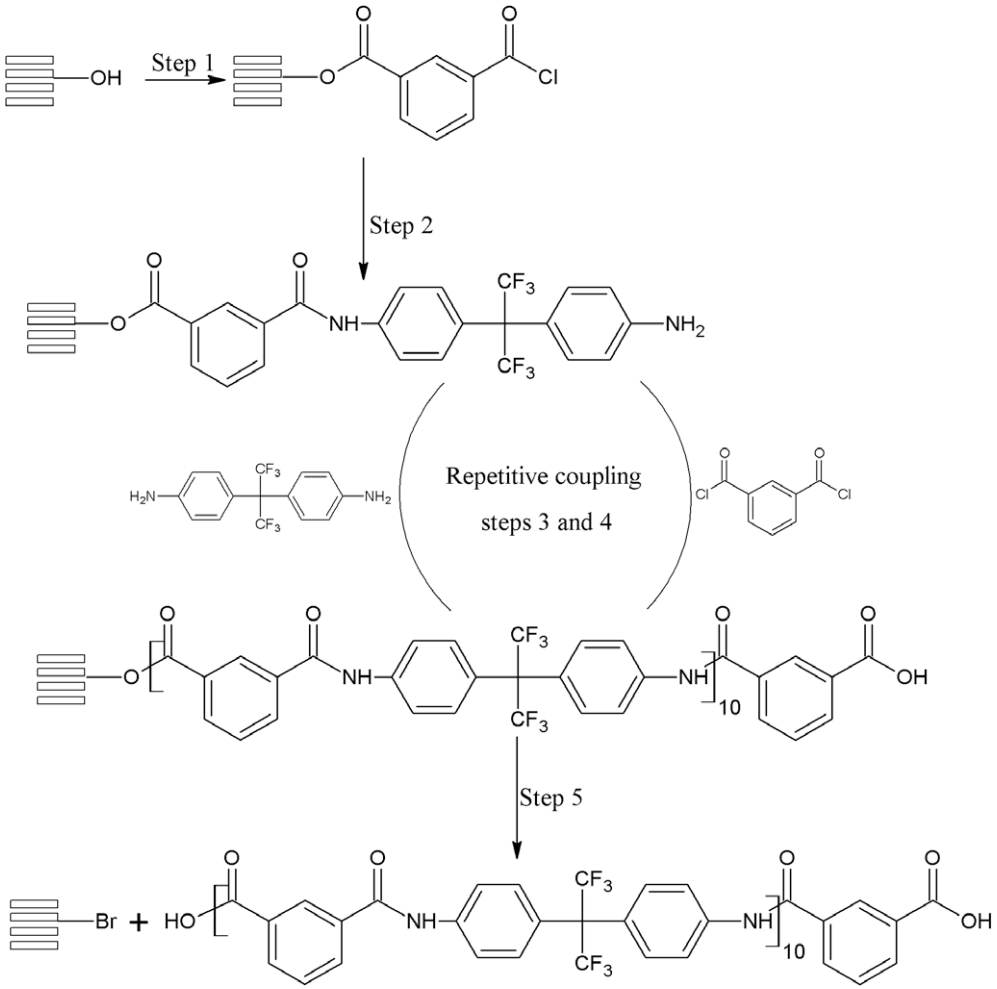

Fig. 1. Schematic strategy for the solid phase synthesis of HFA-ISO aromatic oligoamides.

thermobalance TGA 7 (Perkin-Elmer, Inc.) under nitrogen atmosphere in the temperature range between 50 and 600 °C with a heating rate of 10 °C/min.

3. Results and discussion

The first solid phase synthesis was carried out by Merrifield [6] using the stepwise addition of protected amino acids to a growing peptide chain which was bound by a covalent bond to a solid resin particle. The covalent bond is very important for the attachment of the first monomer to the solid phase. Among the solid supports available commercially we choose the SynPhase™ Lanterns because they are an open ribbon-like stable structure with a large surface area. They are insoluble in the presence of the solvents used; moreover, they have a controlled concentration of functional groups attached to the surface of each support [15]. In order to evaluate the utility of SynPhase™ Lanterns hydroxymethylated in the solid phase synthesis of aromatic oligoamides, first we carry out a benzoylation reaction using isophthaloyl chloride, which reacted with the hydroxyl groups of the solid support in the presence of triethylamine as an acid acceptor. This reaction was measured by attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy. Fig. 2 shows FTIR spectra of the SynPhase™ Lanterns hydroxymethylated and that of the SynPhase™ Lanterns grafted with isophthaloyl chloride. In this figure it can be observed that after the benzoylation reaction the intensities of the characteristic absorptions of O–H groups at 3400 cm^{-1} in the SynPhase™ Lanterns disappear from the hydroxymethylated support, whereas new peaks emerge due to the presence of ester groups at 1720 cm^{-1} (C=O) and 1240 cm^{-1} (C–O). This result implies that reaction between free hydroxyl groups on the surface of the SynPhase™ Lanterns and acyl groups of isophthaloyl chloride has taken place with the formation of an ester bond [13].

The synthesis of oligo(hexafluoro-isopropylidene isophthalamide) (oligo HFA-ISO) was carried out by a series of alternating steps by attaching of 4,4′-hexafluoroisopropylidene diamine or isophthaloyl chloride on the growing chain attached to the initial ester bond on the SynPhase™ Lanterns support until reaching the desired polymerization degree n = 10. The use of symmetric nonprotected monomers

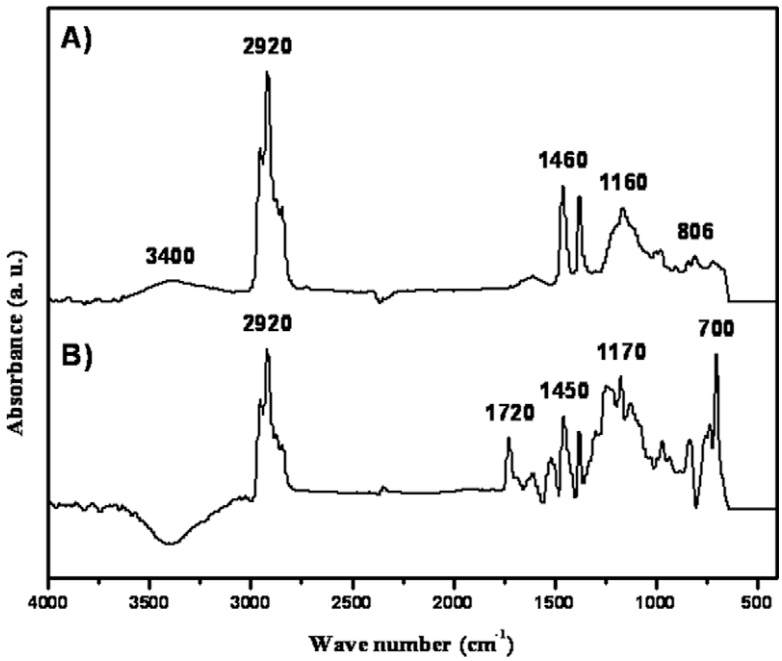

Fig. 2. ATR-FTIR spectrum of hydroxymethylated (A) and benzoylated SynPhase™ Lanterns (B).

simplifies the reaction and decrease the number of coupling steps as compared to the reported oligo(*p*-benzamide) reactions [12]. Furthermore, on each coupling step the reaction was enforced by employing a high excess (1:10) of each particular monomer [13,14]. On the other hand, the low concentration of –OH groups on the SynPhase™ Lanterns supports decreases the probability of having chain to chain coupling reactions, which has been previously reported [13]. Moreover, the chain stiffness of HFA-ISO aromatic oligoamides will decrease the flexibility of amide bond rotation, and thereby also helps to avoid chain to chain coupling reactions. Another, advantage of the use of this solid support is that the reactions take place on the surface of the solid support [15], enhancing the contact between the monomer and the growing oligomer chain, while in the Wang resin to carry out the reaction it requires the penetration of solvent and monomers into the resin matrix.

The HFA-ISO oligoamides were cleaved from the support with a 33% (w/v) hydrogen bromide in acetic acid solution that was neutralized in methanol and precipitated in water. This material was dissolved in DMF with 4.5% (w/v) LiCl and the molecular weight and molecular weight distribution evaluated by GPC. The synthesis of HFA-ISO aromatic oligoamides on SynPhase™ Lanterns supports was carried out by duplicate and the GPC determinations in both cases only show one distribution peak as depicted in Fig. 3. The weight average molecular weight ($\overline{M}_w$) detected was 5.48×10^3 g/mol and the number average molecular weight ($\overline{M}_n$) was 5.32×10^3 g/mol relative to PS standards. Therefore, the polydispersity index (PDI) of the HFA-ISO oligoamides was 1.03, this finding confirms that the solid phase synthesis can be used to synthesize HFA-ISO aromatic oligoamides with controlled molecular weight and narrow molecular weight distribution. Since the $\overline{M}_w$ obtained was almost identical to $\overline{M}_w$ calculated by HFA-ISO oligoamides of $n = 10$, it is clear that the control in the molecular weight was successfully obtained in this work. Solid phase organic synthesis of nonbiological oligomers has advantages over the solution-phase methods with respect to sequence control, ease of purification, and speed. The products can be well-defined oligomers that are not possible to obtained in the polymer syntheses by classical polycondensation where the statistical distribution of reactions lead to a broad distribution of molecular weights and chain sizes [16,17]. Utilizing this same approach with a Wang resin König et al. [12] reported the synthesis of an oligo(*p*-benzamide) of 10 units with 10 coupling steps and 10 Fmoc deprotection steps. On another report, Hartmann et al. [14] achieved 8 coupling cycles using a stepwise reaction of dicarboxylates and diamines to synthesize poly(amidoamines) with controlled segment length.

The chemical nature of the HFA-ISO aromatic oligoamides was evaluated using FTIR and ^{1}H-NMR. Fig. 4 shows the FTIR spectrum of HFA-ISO oligoamides. It presents intensities of the characteristic peaks that agree with those reported for the standard polycondensation to obtain HFA-ISO aromatic polyamides [3], a carbonyl absorption band at 1660 cm^{-1} and a broad absorption band attributed to the amine group at 3300 cm^{-1}. The ^{1}H-NMR confirms the chemical structure of the HFA-ISO aromatic oligoamide (Fig. 5). The singlet at 11.77 and 11.53 ppm are attributed to the amide bond –NH–, the peaks between 7.0 and 9.0 ppm are characteristic of the protons of the phenyl groups while the singlet at 9.56 ppm is attributed to the terminal OH– groups in the oligomer, this fact may render them as potential candidates for building block copolymers

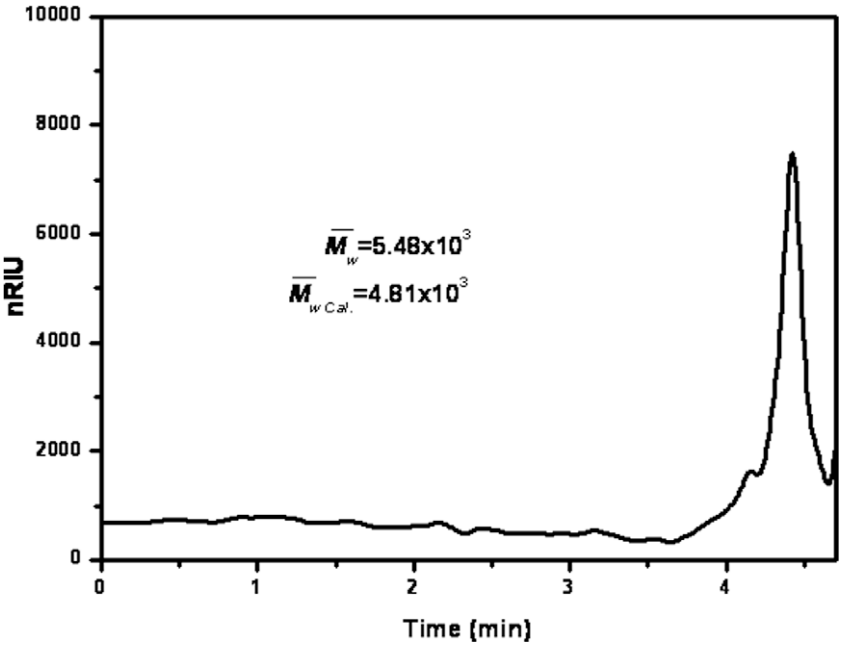

Fig. 3. GPC profile of monodisperse HFA-ISO aromatic oligoamides.

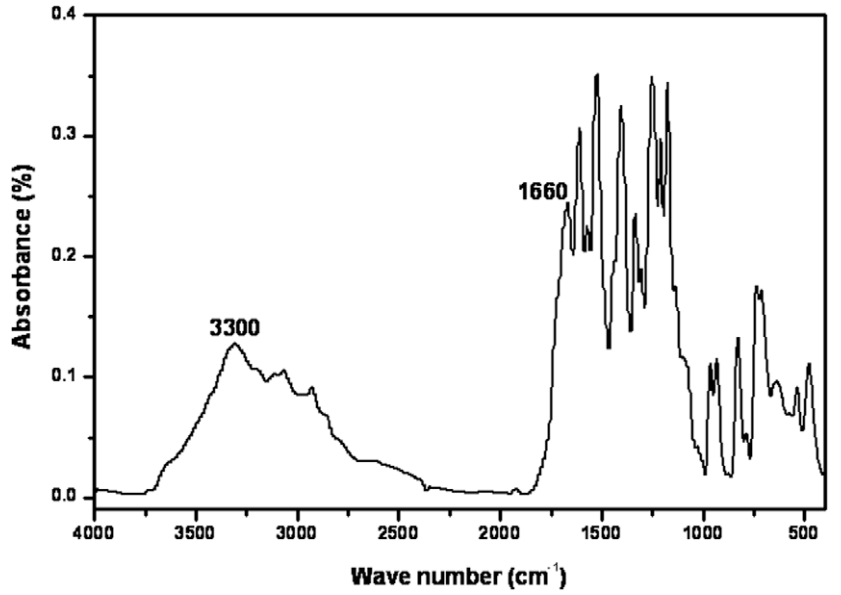

Fig. 4. FTIR spectrum of the HFA-ISO aromatic oligoamides.

[18,19]. It is also interesting to point out that the absence of peaks in the range of 5.5–4.5 ppm confirmed that the HFA-ISO aromatic oligoamides have not terminal NH_2-amine groups [20]. The molecular weight determined by GPC and ^{1}H-NMR measurements was in close agreement. An internal calculation of the ratio of amine in the skeletal bond –NH– to –OH terminal groups in the HFA-ISO aromatic oligoamides structure indicates that there are 8.4 –NH– groups for each –OH group. This would indicate that there are nine repeating units on each oligomer. Taking into account the uncertainty involved in ^{1}H-NMR measurements it will confirm that the target number of units was closely achieved.

The thermal properties of a HFA-ISO aromatic oligoamides were evaluated by TGA and DSC. The glass transition temperature, T_g, observed for the HFA-ISO oligoamides was 188 °C (Fig. 6). The sharpness of the transition indicates that there is little polydispersity in the sample. The lower T_g value for the aromatic oligoamides has been expected as indicative for their lower molecular weight as compared

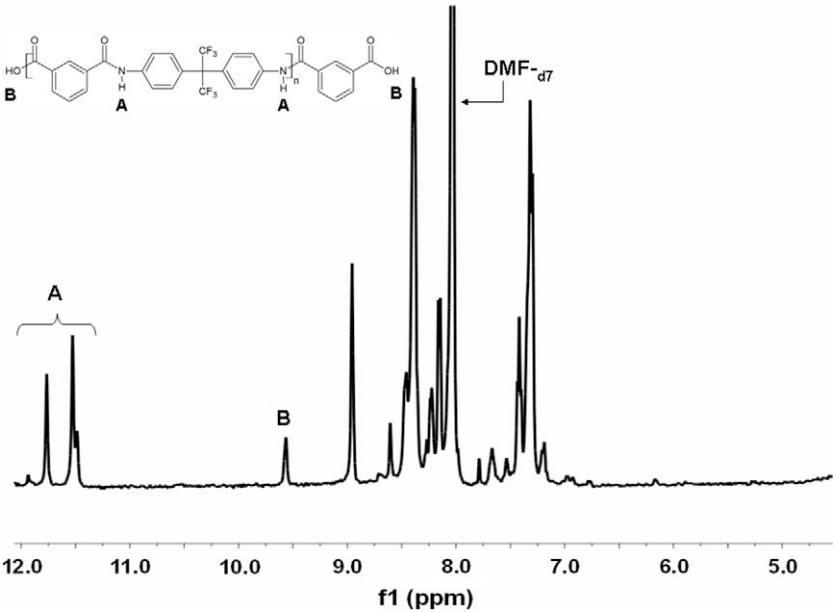

Fig. 5. ^{1}H-NMR spectrum of the HFA-ISO aromatic oligoamides.

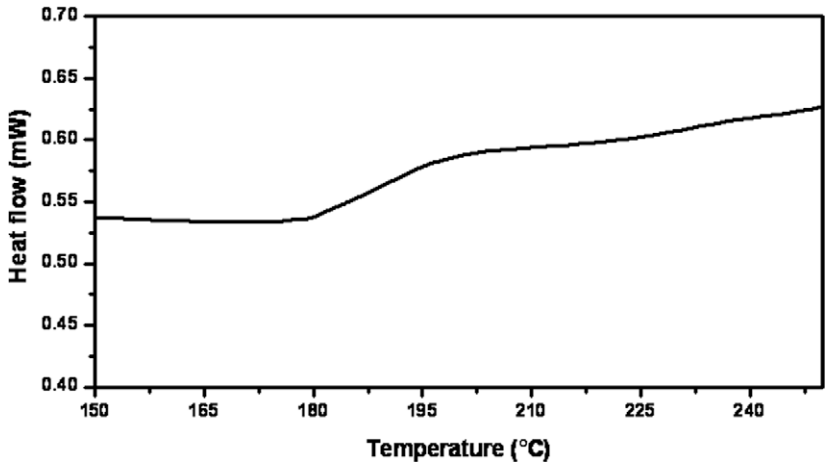

Fig. 6. DSC trace of HFA-ISO oligoamides (second heating run at a scan rate of 10 °C/min using 5.0 mg samples under a nitrogen atmosphere).

to that of the aromatic HFA-ISO polyamides of high molecular weight ($\overline{M}_w = 1.23 \times 10^5$) that have T_g values in the range of 272–303 °C [2,3,21]. Moreover, it was reported that the T_g of aromatic polyamides increase sharply up to a certain critical molecular weight and then appears to be virtually unaffected by further increases in molecular weight [22]. The thermal stability of the HFA-ISO aromatic oligoamides was evaluated by TGA, and the thermogram for their decomposition is shown in Fig. 7. Taking the onset of decomposition temperature ($T_{d,onset}$) as a criterion of thermal stability, the HFA-ISO aromatic oligoamides with $n = 10$ display a $T_{d,onset}$ at 388 °C which is less stable than the corresponding reference HFA-ISO polyamides ($T_{d,onset}$ = 492 °C) [3]. Moreover, the HFA-ISO oligoamides present a 38% weight loss at 500 °C while the maximum weight loss reported by HFA-ISO aromatic polyamides at this temperature was 11% [3]. These results indicate that the lower molecular weight diminishes the thermal stability in the oligoamides.

4. Conclusion

In summary, we have described the stepwise preparation of HFA-ISO aromatic oligoamides with controlled molecular weight and a narrow molecular weight distribution (PDI = 1.03). The synthesis of the oligomers was carried out on a solid support of SynPhase™ Lanterns Hydroxymethylated. In this procedure the stepwise growth of HFA-ISO aromatic oligoamides was carried out by subsequent coupling steps of diamines with diacyl chlorides. This procedure allowed good control over the molecular weight and

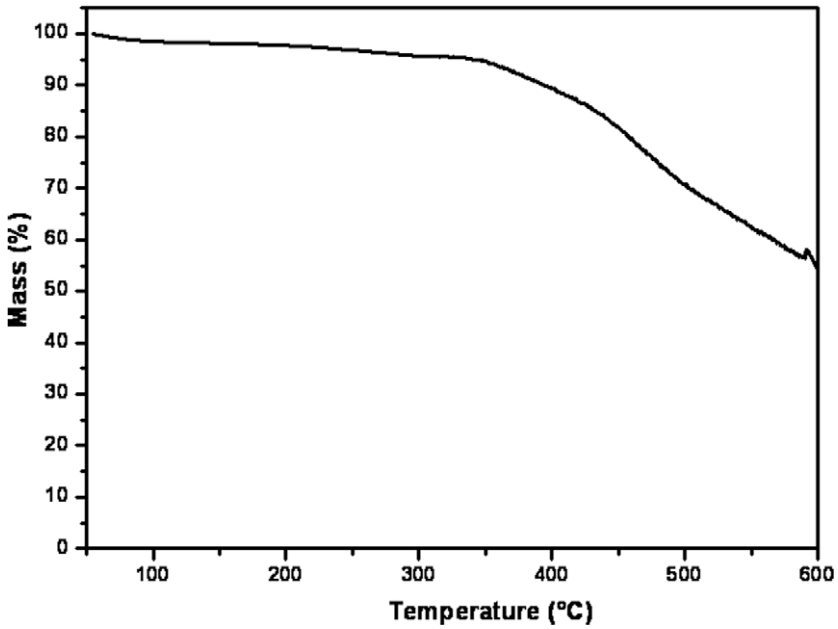

Fig. 7. TGA thermogram of the HFA-ISO aromatic oligoamides.

polydispersity of HFA-ISO segments as demonstrated by GPC. In addition, this strategy permitted a good efficiency in the HFA-ISO aromatic oligoamides building-up with OH-end groups as confirmed by FTIR and ^{1}H-NMR. This solid phase supported synthesis approach, including the alternating coupling steps, provides the opportunity to design and produce well-defined building blocks with defined functionality and properties. Moreover, these HFA-ISO aromatic oligoamides should be useful for applications in the synthesis of block copolymers allowing the study of relationships between chain length and physical properties in block copolymer systems.

Acknowledgements

J.L. Santiago-Garcia acknowledges a scholarship (191574) by CONACyT to carry out Ph.D. studies. This research was performed under Grant No. 41437 CONACyT-México.

References

[1] Negi YS, Razdan U, Saran V. Soluble aromatic polyamides and copolyamides. JMS Rev Macromol Chem Phys 1999;39:391–493.
[2] Shing A, Ghosal K, Freeman BD, Lozano AE, de la Campa JG, de Abajo J. Gas separation properties of pendent phenyl substituted aromatic polyamides containing sulfone and hexafluoroisopropylidene groups. Polymer 1999;40:5715–22.
[3] Carrera-Figueiras C, Aguilar-Vega M. Gas permeability and selectivity of hexafluoroisopropylidene aromatic isophthalic copolyamides. J Polym Sci B Polym Phys 2005;43:2625–38.
[4] Higashi F. Activated polycondensation. In: Mijs WJ, editor. New methods for polymer synthesis. New York: Plenum Press; 1992. p. 211–36.
[5] Rogers ME, Long TE, Turner SR. Introduction to synthetic methods in step-growth polymers. In: Rogers ME, Long TE, editors. Synthetic methods in step-growth polymers . John Wiley & Sons, Inc.; 2003. p. 1–16.
[6] Merrifield RB. Solid phase peptide synthesis: I. The synthesis of tetrapeptide. J Am Chem Soc 1963;65:2149–54.
[7] Hawker CJ, Wooley KL. The convergence of synthetic organic and polymer chemistries. Science 2005:1200–5.
[8] Prontello JK, Allen MJ, Underbakke ES, Kiessling LL. Solid-phase synthesis of polymers using the ring-opening metathesis polymerization. J Am Chem Soc 2005;127:14536–67.
[9] Mei Y, Beers KL, Byrd HC, VanderHart DL, Washburn NR. Solid-phase ATRP synthesis of peptide–polymer hybrids. J Am Chem Soc 2004;126:3472–6.
[10] Nelson JC, Young JK, Moore JS. Solid-phase synthesis of phenylacetylene oligomers utilizing a novel 3-propyl-3-(benzyl-supported) triazene linkage. J Org Chem 1996;61:8160–8.
[11] Baird EE, Dervan PB. Solid phase synthesis of polyamides containing imidazole and pyrrole amino acids. J Am Chem Soc 1996;118:6141–6.
[12] König HM, Abbel R, Schollmeyer D, Kilbinger AFM. Solid-phase synthesis of oligo(*p*-benzamide) foldamers. Org Lett 2006;8:1819–22.
[13] Nakata S, Brisson J. Monodisperse polyamide oligomers: a facile synthesis of small polyamide oligomers on a solid polymer support. Eur Polym J 2000;36:831–9.
[14] Hartmann L, Krause E, Antonietti M, Börner HG. Solid-phase supported polymer synthesis of sequence-defined multifunctional poly(amidoamines). Biomacromolecules 2006;7:1239–44.
[15] Parsons JG, Sheehan CS, Wu Z, James IW, Bray AM. A review of solid-phase organic synthesis on SynPhase? Lanterns and SynPhase? Crowns Methods Enzymol 2003;369:39–73.
[16] Moore JF, Hill DJ, Mio MJ. Solid-phase synthesis of sequence-specific phenylacetylene oligomers. In: Burgess K, editor. Solid-phase organic synthesis. New York: John Wiley & Sons, Inc.; 2000. p. 119–47.
[17] Dörwald FZ. Organic synthesis on solid phase: supports, linkers, reactions. 2nd ed. Weinheim: Wiley-VCH; 2002.
[18] Abbel R, Frey H, Schollmeyer D, Kilbinger AFM. Soluble oligoaramide precursors – a novel class of building blocks for rod-coil architectures. Chem Eur J 2005;11:2170–6.
[19] van Domeselaar GH, Kwon GS, Andrew LC, Wishart DS. Application of solid phase synthesis to engineering PEO-peptide block copolymers for drug delivery. Colloids Surf B 2003;30:323–34.
[20] Korematsu A, Furuzono T, Kishid A. Synthesis of block copolymers containing chain-controlled aramid and fluoroethylene segments. Macromol Mater Eng 2005;290:66–71.
[21] Palí R, Loría-Bastarrachea M, Aguilar-Vega M, Angulo JL, Vazquez H. Synthesis and characterization of aromatic polyamides obtained from 4-4′-(9-fluorenylidene)diamine, 4-4′-(hexafluoroisopropylidene)dianiline and 4-4′-diamine-benzophenone. High Perform Polym 2002;14:77–91.
[22] Khanna YP, Pearce EM. Aromatic polyamides. VI: molecular weight effects on thermal properties. J Polym Sci Polym Chem Ed 1986;24:2377–81.