Articles

Novel Polyanhydrides with Enhanced Thermal and Solubility Properties

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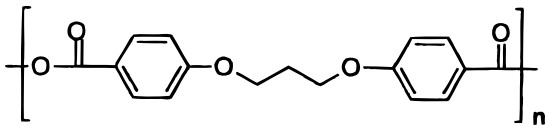
ABSTRACT: A series of polyanhydrides based on *o*-, *m*-, and *p*-xylenes as derived from *o*- and *p*-hydroxybenzoic acids were synthesized by melt-condensation polymerization. Precursors, monomers, and polymers were characterized by NMR and IR spectroscopies, elemental and thermogravimetric analyses, and thermal transition temperatures. Polymers containing *p*-xylenes and *p*-hydroxybenzoic acids were relatively insoluble with high T_g's. In contrast, polymers containing *o*- and *m*-xylyl moieties based on *o*-hydroxybenzoic acids exhibit good solubilities and T_g's below 100 °C.

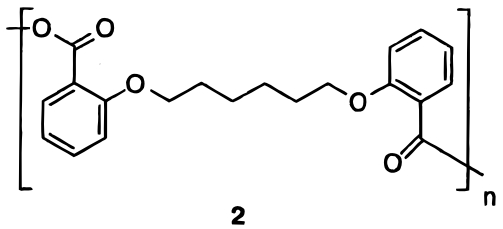
Introduction

Polyanhydrides containing 1,3-bis(*p*-carboxyphenoxy)-propane (**1**) are hydrolytically degradable polymers currently used in implanted devices to control the delivery of chemotherapeutic drugs.[1] Polyanhydrides based on **1** demonstrate zero-order release kinetics[2] and erode by surface-erosion processes.[3] While these aromatic polyanhydrides have excellent biocompatibility characteristics, they are insoluble in many common organic solvents and melt at high temperatures,[2,4,5] characteristics that can limit the fabrication of these polymers into biomedical devices.



1

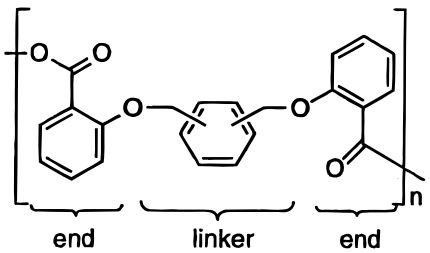
To improve the solubility and thermal processing characteristics, we synthesized a related family of novel aromatic polyanhydrides in which the ring substitution pattern of **1** was modified from para to ortho substitution (**2**).[6]



2

We observed enhanced solubility in low boiling organic solvents while maintaining the desirable characteristics of biodegradability, biocompatibility, and mechanical strength.[6,7] Although these findings represent an improvement over polyanhydrides such as **1**, the thermal properties of **2** may limit its use as a biomaterial: the glass transition temperature of the ortho-substituted polyanhydride (**2**) is 34 °C, slightly below physiological temperature of 37 °C. For drug delivery devices such as fibers or microspheres, the inability to retain a shape over time does not allow for accurate calculations of drug delivery rates. Surface eroding polymers such as polyanhydrides can release drugs in a predictable manner based on size and shape.[8]

To increase the glass transition temperature while maintaining solubility, alternate aromatic moieties were incorporated into the polymer backbone of **2**. Ortho-, meta-, and para-substituted xylenes were chosen to replace the alkyl chains of **2** to give polymer **3** because of the facile chemistry of benzylic carbons and to increase the rigidity of the polymer. Xylyl ether moieties have been investigated as components of pharmacologic and medicinal compounds.[9−12]



3 a:*ortho-*
b:*meta-*
c:*para-*

In this report, we describe the synthesis and characterization of a series of polyanhydrides containing repeat units with ortho-substituted "ends" and either ortho- , meta- , or para-substituted xylyl groups as "linkers" (**3**). We define "ends" as the aromatic rings substituted with carboxyl groups; there are two "ends" per repeat unit, and "linkers" refers to the connecting aromatic ring. Additional polyanhydrides with repeat units of para-substituted ends and either ortho-, meta-, or para-substituted xylyl linkers (**4**) were prepared to generate polymers with optimal properties for use as

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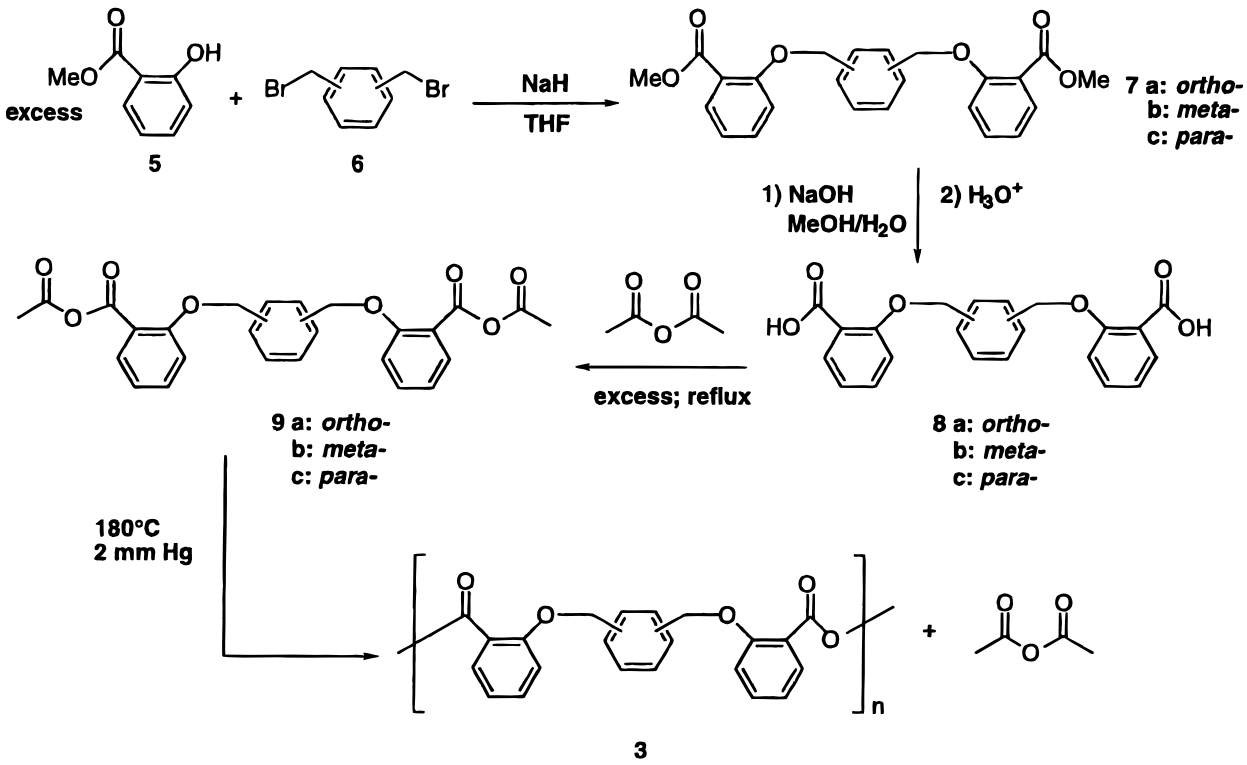
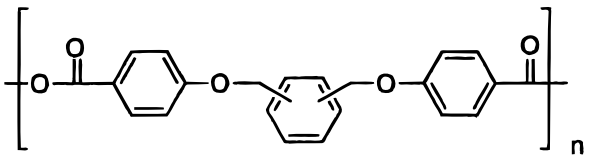
Scheme 1



drug delivery devices.



4 a:*ortho-*
b:*meta-*
c:*para-*

Results and Discussion

A series of xylene-based polyanhydrides (**3** and **4**) were synthesized in which the ring substitution patterns were varied for both the linkers and ends of the polymer repeat units. This article describes the synthesis and details the physicochemical changes as a function of polymer backbone configuration.

A synthetic method for only diacids based on polymer **3** was patented in 1967 by Kobayashi et al.[13] As described by Kobayashi, the coupling reaction was performed in aqueous methanol, with potassium hydroxide as base and salicylic acid as starting material. The product was isolated after addition of the appropriate dichloroxylene and acidification. Our attempts at this method resulted in low yields of isolated diacids (**8**). We subsequently developed our own synthetic approach as outlined in Scheme 1. In brief, *o*-hydroxy methyl esters (**5**) were coupled to dibromoxylene (**6**) to yield methyl esters (**7**), which were hydrolyzed to give the free diacid (**8**). Acetylation of the carboxylic acid groups of **8** yielded the monomer (**9**). Using previously established polymerization conditions,[6] polyanhydrides (**3**) were prepared by melt condensation of **9**.

Polyanhydrides Derived from *o*-Carboxyphenoxyxylenes (3). The properties of polymers with ortho-substituted end groups and either ortho-, meta-, or para-substituted xylyl groups as linkers (**3**) are summarized in Table 1. Qualitative and quantitative solubilities are shown in Table 2.

Table 1. Characteristics of *o*-Carboxyphenoxyxylenes (3)

polymer	xylyl substitution	M_w	PDI	T_g (°C)	T_m (°C)	T_d (°C)
3a	ortho	19000	2.2	82	*a*	340
3b	meta	6900	2.0	71	*a*	350
3c	para	*b*	*b*	84	114	320

[a] Not observed. [b] Insoluble.

Table 2. Qualitative and Quantitative Solubilities of Polyanhydrides[a]

polymer	DMF	THF	CH_2Cl_2
3a	++	++	>500 mg/mL
3b	++	++	880 mg/mL
3c	++	−	>600 mg/mL
4a	+	+	+
4b	−	−	−

[a] Symbols: ++ = soluble, + = slightly soluble, and − = insoluble.

The molecular weights as determined by gel permeation chromatography (GPC) decreased as the xylyl substitution was changed from ortho to meta, while the polydispersity index (PDI) remained relatively unchanged. The polymer with the *p*-xylyl link (**3c**) was insoluble in THF, the eluting solvent for GPC. Because our goal is to increase thermal properties while maintaining solubility in common organic solvents (i.e., THF, methylene chloride), polymers based on **3c** were not pursued further.

Glass transition (T_g) and melting (T_m) temperatures were determined by differential scanning calorimetry (DSC). The T_g's for ortho- and para-linked polymers were similar (82 and 84 °C, respectively) while the T_g for the meta-linked polymer was lower by ∼10 °C. The presence of the *o*-xylyl linker, in conjunction with the

Chart 1

10 **a:*ortho-***
b:*meta-*
c:*para-*

11 **a:*ortho-***
b:*meta-*

12 **a:*ortho-***
b:*meta-*

Table 3. Characteristics of *p*-Carboxyphenoxyxylenes

polymer	xylyl substitution	M_w	PDI	T_g (°C)	T_m (°C)	T_d (°C)
4a	ortho	10900	1.9	101	*a*	370
4b	meta	*b*	*b*	89	226[c]	380

[a] Not observed. [b] Insoluble. [c] First run only.

ortho ends, forms a regularly repeating pattern of ortho substitution that may promote polymer−polymer interactions, thus increasing T_g. In the para variant, linearity of the linkers allows for a higher degree of polymer packing and thus a higher T_g as well as enhanced T_m. The absence of a T_m for the ortho and meta variants indicates that crystallinity is disrupted by the nonlinearity of these linkers. The decomposition temperature (T_d) of the polymers as measured by thermal gravimetric analysis (TGA) is not significantly affected by changing the linker substitution pattern.

Polyanhydrides Derived from *p*-Carboxyphenoxyxylenes (4). As comparison for the *o*-xylene-based polymers (**3**), polymers consisting of para-substituted ends with either *o*-, *m*-, or *p*-xylyl groups as linkers were synthesized. Structures for the methyl ester derivative (**10**), diacid (**11**), and monomer (**12**) are shown in Chart 1. Polymer properties of **4** are shown in Table 3. Solubilities are shown in Table 2.

GPC analysis was only performed on the ortho variant (**4a**) because **4b** was insoluble in THF. The para variant of the diacid (**11**) could not even be synthesized due to insolubility of its methyl ester (**10c**) in solvents such as DMSO, DMF, THF, methanol, and methylene chloride.

As observed in the previous polymer systems (**3**), changing the linker substitution pattern from ortho to meta decreases the T_g by 12 °C. A T_m is only observed for the meta variant (**4b**). As described previously, changes in the linker substitution pattern do not significantly affect T_d.

Conclusion

A series of polyanhydrides based on xylenes were synthesized by melt-condensation polymerization. When comparing the characteristics of these polymers, thermal and solubility properties directly correlate to the chemical composition of the polymer backbone. For example, when the polymer is amorphous (i.e., no observed T_m), the solubility properties remain unaffected. However, when T_m is observed, the solubility properties are significantly decreased due to crystallinity. On the basis of our requirement for solubility and T_g's above 37 °C, three systems will be evaluated further: **3a**, **3b**, and **4a**. Degradation and mechanical characteristics are currently under investigation and results reported elsewhere.

Experimental Section

Materials. Diethyl ether, acetic anhydride, and tetrahydrofuran (THF) were obtained from Fisher. THF was distilled before use. All other chemicals were purchased from Aldrich and used as received.

Methods. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Varian 200 MHz spectrometer. Samples (5−10 mg) were dissolved in DMSO-d_6 with the solvent as the internal reference. Infrared (IR) spectra were measured on a Mattson Series spectrophotometer by solvent-casting samples onto a KBr plate. Elemental analyses were provided by QTI (Whitehouse, NJ).

Molecular weights (M_w) and polydispersity index (PDI) were determined on a Perkin-Elmer (PE) LC system consisting of a series 200 refractive index detector, a series 200 LC pump, and ISS 200 autosampler. A DEC Celebris 466 computer running PE Turbochrom 4 software was used for data collection and processing and to automate the analysis via a PE Nelson 900 interface and PE Nelson 600 link. Samples were resolved on a PE PL-Gel column (5 μm, mixed bed) at 30 °C, with THF as eluent at a flow rate of 0.5 mL/min. Samples (5 mg/mL) were dissolved into THF and filtered using 0.45 μm PTFE syringe filters prior to elution. Molecular weights were calibrated relative to narrow molecular weight polystyrene standards (Polysciences, Dorval, Canada).

Thermal analysis was performed on a Perkin-Elmer system consisting of Pyris 1 DSC and TGA 7 analyzers with TAC 7/DX instrument controllers. PE Pyris software was used for data collection and processing on a DEC Venturis 5100 computer. For DSC, samples (5 mg) were heated under dry nitrogen gas. Data were collected at heating and cooling rates of 15 °C/min with a three-cycle minimum. For TGA, samples (10 mg) were heated under dry nitrogen gas. Data were collected at a heating rate of 20 °C/min. Decomposition temperatures were defined as the onset of decomposition.

Melting points below 200 °C were determined on a Thomas-Hoover apparatus, while those above 200 °C were determined on the Pyris 1 DSC (see above).

Quantitative solubilities were determined on a Perkin-Elmer Lambda 40 UV spectrometer. PE UV WinLab software running on a Dell Optiplex GX1 computer was used to control the instrument and analyze the data. Standards were prepared by dissolving a known weight of the appropriate polymer in methylene chloride to concentrations of magnitude 10^{-2}−10^{-3} mg/mL and analyzed in 10 mm path length quartz cuvettes. Saturated solutions were prepared in a similar manner. From the absorbance values of the standards, a calibration curve was derived from which the concentrations of the saturated polymer solutions were calculated. Qualitative solubilities were performed visually by mixing polymer and solvent in a test tube and then observing the clarity or turbidity of the solution.

Preparation of Methyl Ester Derivatives (7). A typical procedure follows. Sodium hydride (46 mmol) was added to an ice-cold solution of the appropriate hydroxybenzoic acid (ortho or para) (45.5 mmol) dissolved in dry THF (40 mL). For the para-substituted materials a small amount of *N*,*N*-dimethylformamide (DMF) (10 mL) was necessary to solubilize the hydroxybenzoate. The reaction mixture was heated to reflux temperature before the appropriate xylene (ortho, meta, or para) (11.4 mmol) was added over the course of 0.5 h. The reaction mixture was heated at reflux temperature overnight (∼12 h). After cooling, NaBr was removed by filtration, the filtrate was evaporated to dryness and acidified with 2 N HCl-(aq), and the product was isolated by decanting off the aqueous

portion. Product was purified by washing with hexanes (if oil) or ethyl acetate (if solid).

α,α′-Bis(*o*-carboxyphenoxy)-*o*-xylene Methyl Ester (7a). Yield: 52% (yellow oil). ^{1}H NMR (DMSO-d_6): δ 7.74 (m, 4H, ArH), 7.55 (t, 2H, ArH), 7.43 (m, 2H, ArH), 7.30 (d, 2H, ArH), 7.06 (t, 2H, ArH), 5.40 (s, 4H, CH_2), 3.80 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1715 (C═O), 1600 (Ar−O−C), 1245 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 70.58; H, 5.61.

α,α′-Bis(*o*-carboxyphenoxy)-*m*-xylene Methyl Ester (7b). Yield: 53% (yellow oil). ^{1}H NMR (DMSO-d_6): δ 7.70 (d, 2H, ArH), 7.60 (t, 2H, ArH), 7.48 (s, 3H, Ar′H), 7.29 (d, 2H, ArH), 7.07 (t, 2H, ArH), 5.26 (s, 4H, CH_2), 3.82 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1725 (C═O), 1600 (Ar−O−C), 1250 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 68.27; H, 5.60.

α,α′-Bis(*o*-carboxyphenoxy)-*p*-xylene Methyl Ester (7c). Yield: 55% (white solid). ^{1}H NMR (DMSO-d_6): δ 7.70 (d, 2H, ArH), 7.55 (s, 4H, ArH), 7.50 (m, 2H, ArH), 7.25 (d, 2H, ArH), 7.05 (t, 2H, ArH), 5.24 (s, 4H, CH_2), 3.82 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1720 (C═O), 1695 (Ar−O−C), 1245 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 62.77; H, 4.94. T_m = 120−122 °C.

α,α′-Bis(*p*-carboxyphenoxy)-*o*-xylene Methyl Ester (10a). Yield: 69% (white solid). ^{1}H NMR (DMSO-d_6): δ 7.90 (d, 4H, ArH), 7.55 (s, 2H, ArH), 7.40 (s, 2H, ArH), 7.15 (d, 4H, ArH), 5.34 (s, 4H, CH_2), 3.82 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1715 (C═O), 1605 (Ar−O−C), 1280 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 70.59; H, 5.68. T_m = 138−140 °C.

α,α′-Bis(*p*-carboxyphenoxy)-*m*-xylene Methyl Ester (10b). Yield: 35% (yellow solid). ^{1}H NMR (DMSO-d_6): δ 8.00 (d, 4H, ArH), 7.65 (s, 1H, ArH), 7.55 (s, 3H, ArH), 7.22 (d, 4H, ArH), 5.31 (s, 4H, CH_2), 3.91 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1720 (C═O), 1605 (Ar−O−C), 1285 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 69.59; H, 5.40. T_m = 133−135 °C.

α,α′-Bis(*p*-carboxyphenoxy)-*p*-xylene Methyl Ester (10c). Yield: 84% (tan solid). ^{1}H NMR data unavailable due to insolubility of compound in organic solvents. IR (KBr, cm^{-1}): 1715 (C═O), 1605 (Ar−O−C), 1280 (C−O). Anal. Calcd: C, 70.92; H, 5.46. Found: C, 69.31; H, 5.48. T_m = 199−202 °C.

Preparation of Diacids. The methyl ester (**7**) (3.4 mmol) was added to a 10:1 methanol:water mixture (200 mL). Sodium hydroxide pellets were added, pH > 12 (124 mmol). The reaction mixture was heated to reflux temperature for 1 h, cooled, and acidified with 2 N HCl(aq) to pH 1. The methanol was removed by rotoevaporation, and the precipitate was filtered and washed with water.

α,α′-Bis(*o*-carboxyphenoxy)-*o*-xylene Diacid (8a). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 7.70 (d, 4H, ArH), 7.50 (t, 2H, ArH), 7.40 (q, 2H, ArH), 7.25 (d, 2H, ArH), 7.05 (t, 2H, ArH), 5.40 (s, 4H, CH_2). IR (KBr, cm^{-1}): 2920 (O−H), 1675 (C═O), 1600 (Ar−O−C), 1320 (C−O). Anal. Calcd: C, 69.83; H, 4.80. Found: C, 69.88; H, 5.08. T_m = 172−175 °C.

α,α′-Bis(*o*-carboxyphenoxy)-*m*-xylene Diacid (8b). Yield: quantitative (yellow solid). ^{1}H NMR (DMSO-d_6): δ 7.65 (m, 3H, ArH), 7.47 (m, 5H, ArH), 7.20 (d, 2H, ArH), 7.03 (t, 2H, ArH), 5.22 (s, 4H, CH_2). IR (KBr, cm^{-1}): 3285 (O−H), 1695 (C═O), 1600 (Ar−O−C), 1255 (C−O). Anal. Calcd: C, 69.83; H, 4.80. Found: C, 69.30; H, 5.03. T_m = 146−150 °C.

α,α′-Bis(*o*-carboxyphenoxy)-*p*-xylene Diacid (8c). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 12.65 (s, 2H, −COOH), 7.70 (d, 2H, ArH), 7.55 (s, 4H, ArH), 7.55 (m, 2H, ArH), 7.20 (d, 2H, ArH), 7.05 (t, 2H, ArH), 5.23 (s, 4H, CH_2). IR (KBr, cm^{-1}): 3245 (O−H), 1720 (C═O), 1600 (Ar−O−C), 1295 (C−O). Anal. Calcd: C, 69.83; H, 4.80. Found: C, 69.43; H, 5.03. T_m = 238 °C.

α,α′-Bis(*p*-carboxyphenoxy)-*o*-xylene Diacid (11a). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 7.89 (d, 4H, ArH), 7.55 (s, 2H, ArH), 7.40 (s, 2H, ArH), 7.10 (d, 4H, ArH), 5.34 (s, 4H, CH_2). IR (KBr, cm^{-1}): 2920 (O−H), 1680 (C═O), 1605 (Ar−O−C), 1265 (C−O). Anal. Calcd: C, 69.83; H, 4.80. Found: C, 69.87; H, 4.95. T_m = 318 °C.

α,α′-Bis(*p*-carboxyphenoxy)-*m*-xylene Diacid (11b). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 7.90 (d, 4H, ArH), 7.50 (s, 1H, ArH), 7.45 (s, 3H, ArH), 7.10 (d, 4H, ArH), 5.10 (s, 4H, CH_2). IR (KBr, cm^{-1}): 2900 (O−H), 1670 (C═O), 1605 (Ar−O−C), 1265 (C−O). Anal. Calcd: C, 69.83; H, 4.80. Found: C, 69.32; H, 4.97. T_m = 294 °C.

Preparation of Acetylated Monomers (9). The diacid **8** (3.4 mmol) was activated using an excess amount of acetic anhydride (150 mL) under nitrogen and heated to reflux temperatures. After 2.5 h, the reaction mixture was cooled and evaporated to dryness.

Acetylated α,α′-Bis(*o*-carboxyphenoxy)-*o*-xylene (9a). Yield: quantitative (brown oil). ^{1}H NMR (DMSO-d_6): δ 7.90 (d, 2H, ArH), 7.70 (m, 4H, ArH), 7.35 (m, 4H, ArH), 7.10 (t, 2H, ArH), 5.44 (s, 4H, CH_2), 2.10 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1800,1735 (C═O, anhydride), 1600 (Ar−O−C), 1245 (C−O).

Acetylated α,α′-Bis(*o*-carboxyphenoxy)-*m*-xylene (9b). Yield: quantitative (yellow oil). ^{1}H NMR (DMSO-d_6): δ 7.90 (d, 2H, ArH), 7.70 (t, 3H, ArH), 7.50 (s, 3H, ArH), 7.35 (d, 2H, ArH), 7.15 (t, 2H, ArH), 5.30 (s, 4H, CH_2), 2.08 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1800, 1735 (C═O, anhydride), 1600 (Ar−O−C), 1245 (C−O).

Acetylated α,α′-Bis(*o*-carboxyphenoxy)-*p*-xylene (9c). Yield: quantitative (tan solid). ^{1}H NMR (DMSO-d_6): δ 7.90 (d, 2H, ArH), 7.70 (t, 2H, ArH), 7.55 (s, 4H, ArH), 7.35 (d, 2H, ArH), 7.10 (t, 2H, ArH), 5.30 (s, 4H, CH_2), 2.10 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1805, 1735 (C═O, anhydride), 1600 (Ar−O−C), 1250 (C−O). T_m = 109−111 °C.

Acetylated α,α′-Bis(*p*-carboxyphenoxy)-*o*-xylene (12a). Yield: quantitative (tan solid). ^{1}H NMR (DMSO-d_6): δ 8.00 (d, 4H, ArH), 7.60 (m, 2H, ArH), 7.42 (m, 2H, ArH), 7.20 (d, 4H, ArH), 5.39 (s, 4H, CH_2), 2.37 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1810,1725 (C═O, anhydride), 1605 (Ar−O−C), 1255 (C−O). T_m = 126−130 °C.

Acetylated α,α′-Bis(*p*-carboxyphenoxy)-*m*-xylene (12b). Yield: quantitative (brown oil). ^{1}H NMR (DMSO-d_6): δ 8.10 (d, 4H, ArH), 7.60 (s, 2H, ArH), 7.47 (s, 2H, ArH), 5.29 (s, 4H, CH_2), 2.37 (s, 6H, CH_3). IR (KBr, cm^{-1}): 1805, 1730 (C═O, anhydride), 1605 (Ar−O−C), 1255 (C−O).

Polymerization. The polyanhydrides were synthesized according to methods first described by Conix.[14] Briefly, melt condensation polymerizations were performed on the monomers (500 mg) at 180 °C for 1.5 h under vacuum (2 mmHg) in a jointed test tube containing a magnetic stir bar, attached to a gas−vacuum manifold. The reaction vessel was flushed with dry nitrogen every 15 min with stirring. Polymers were isolated by precipitation into diethyl ether from methylene chloride. M_w, PDI, and thermal properties are given in Tables 1 and 2.

Poly(*o*-COX) (3a). Yield: quantitative (brown solid). ^{1}H NMR (DMSO-d_6): δ 7.75 (b, ArH), 7.45 (b, ArH), 7.14 (b, ArH), 6.90 (b, ArH), 5.23 (b, CH_2). IR (KBr, cm^{-1}): 1780, 1725 (C═O, anhydride), 1600 (Ar−O−C), 1250 (C−O).

Poly(*o*-CMX) (3b). Yield: quantitative (tan solid). ^{1}H NMR (DMSO-d_6): δ 7.80 (b, ArH), 7.50 (b, ArH), 7.25 (b, ArH), 7.10 (b, ArH), 6.95 (b, ArH), 5.05 (b, CH_2). IR (KBr, cm^{-1}): 1780, 1725 (C═O, anhydride), 1600 (Ar−O−C), 1250 (C−O).

Poly(*o*-CPX) (3c). Yield: quantitative (tan solid). ^{1}H NMR (DMSO-d_6): δ 7.80 (d, 2H, ArH), 7.55 (t, 2H, ArH), 7.23 (b, ArH), 6.95 (b, ArH), 5.05 (s, 4H, CH_2). IR (KBr, cm^{-1}): 1780, 1725 (C═O, anhydride), 1600 (Ar−O−C), 1255 (C−O).

Poly(*p*-COX) (4a). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 8.04 (b, 4H, ArH), 7.60 (b, 2H, ArH), 7.42 (b, 2H, ArH), 7.21 (b, 4H, ArH), 5.38 (s, 4H, CH_2). IR (KBr, cm^{-1}): 1780, 1715 (C═O, anhydride), 1605 (Ar−O−C), 1260 (C−O).

Poly(*p*-CMX) (4b). Yield: quantitative (white solid). ^{1}H NMR (DMSO-d_6): δ 8.10 (d, 4H, ArH), 7.60 (s, 2H, ArH), 7.47 (s, 2H, ArH), 7.22 (d, 4H, ArH), 5.29 (s, 4H, CH_2). IR (KBr, cm^{-1}): 1770, 1725 (C═O, anhydride), 1605 (Ar−O−C), 1260 (C−O).

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