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Structure and thermal transitions in a biomedically relevant liquid crystalline poly(ester amide)

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Abstract

There is still a need to develop bioresorbable polymers with high strength and high modulus for load-bearing biomedical applications. Here we investigate the liquid crystalline structural features of poly(desaminotyrosyl-tyrosine dodecyl dodecanedioate), poly(DTD DD), a new bioresorbable poly(ester amide) that is currently studied *in vivo* as a slow-degrading implantable biomaterial for load bearing applications. Thermally induced structural changes in poly(DTD DD) were studied using simultaneously differential scanning calorimetry (DSC) and X-ray scattering. The hexatic SmB organization of the polymer chains that exists at room temperature becomes progressively disordered upon heating, changing into a SmF phase and then into a smectic C phase at 60°C before turning into a free flowing melt at 130°C. X-ray scattering data and thermal analysis indicate the presence of a 2D ordered structure in the polymer melt. A structural model with an interesting 3-fold symmetry in the packing of the side chains around the rigid aromatic main chain, and the packing of these chains into fibrils is proposed. The liquid crystalline behavior of poly(DTD DD) makes it possible to melt process it at low temperatures without thermal degradation. This is a noteworthy advantage for the use of poly(DTD DD) as a high strength, readily processable, yet biodegradable polymer.

Keywords

Poly(ester amide)s; Liquid crystalline phases; Biomedical applications; Thermally-induced structure changes; X-ray scattering

Introduction

Poly(ester amide)s containing derivatives of the natural amino acid L-tyrosine have not been widely used as biomaterials even though some polymers in this family have promising mechanical properties that rival those reported for commonly used polyesters and polycarbonates.^{1, 2} The interchain hydrogen-bonding interactions between amide groups enhance the thermal and mechanical properties, and make it possible to prepare materials that are stronger than the aliphatic polyesters such as poly(ϵ -caprolactone) and polylactide. Because of the presence of the ester group, poly(ester amide) is potentially more degradable

than polycarbonates. Both the strength and the degradability are important in materials to be used in orthopedic and surgical devices.³ These polymers can be functionalized by incorporating α -amino acids with hydroxyl, carboxyl and amine pendant groups, and also by incorporating C=C bonds in both the main chain and in the side groups. Properties such as hydrophilic/hydrophobic ratio and biodegradability can be tuned and a library of poly(ester amide)s polymers can be created for different applications such as controlled drug delivery systems, hydrogels, tissue engineering, and adhesives.^{4, 5}

Processability of polymers is determined by their thermal properties, and the mechanical properties of the processed polymer (e.g., an extruded fiber or an injection molded device) are closely related to the chain conformation and their spatial arrangement.^{6, 7} The properties of poly(ester amides) are determined by the disposition of both the ester and amide groups.^{8–12} In certain instances, the interchain hydrogen bonding of the amide groups gives rise to liquid crystalline (LC) behavior in these polymers. The LC behavior could result from the nature of either the main chain or the side chain,¹³ and could be brought about by changing the temperature in the solid state (thermotropic LC) or the concentration in solution (lyotropic LC). The LC order enhances the stiffness and dimensional stability in otherwise amorphous polymers in the solid state, and lowers the melt viscosity in the fluid phase. Therefore, such LC polymers are highly desirable for many load bearing applications. In particular, their flow properties permit these polymers to be processed easily without degrading the polymer, a major drawback in processing degradable polymers into biomedical devices. For instance, polymers intended for load bearing applications have to be strong (higher modulus and ultimate strength), have low water uptake and hence minimal swelling upon implantation, high dimensional stability, and be easily processable. Polymers with ester and amide linkages meet many of these criteria.^{8, 10, 14–16}

Here we investigate the structure and temperature-dependent phase behavior of poly(desaminotyrosyl-tyrosine dodecyl dodecandioate), poly(DTD DD), which is part of a library poly(ester amide)s (Figure 1).^{4, 17} The physico-mechanical properties of this polymer are better than those of similar polymers that are currently used for biomedical applications.^{5, 18} Therefore, oriented fibers of poly(DTD DD) have been used to create medical implants designed to repair ligament and meniscus. These implants have been tested in animal models^{19, 20} The effect of chemical composition of the polymer on degradability, biocompatibility and cell-material interactions have been well studied,^{4, 21} but the influence of chemistry and the processing conditions on the microstructure is less well understood. Previous studies using differential scanning calorimetry (DSC),^{22–25} thermally stimulated current (TSC)^{22, 23} and FTIR spectroscopy²² have shown that poly(DTD DD) exhibits a liquid crystalline structure. In this study, we discuss the thermotropic liquid crystalline behavior of the polymer by examining the structural changes at multiple length scales (1 to 100 Å) across the various thermal transitions using small-, medium- and wide-angle X-ray scattering (SAXS, MAXS and WAXS) obtained simultaneously during the DSC scans.

Materials and methods

Poly(DTD DD) was synthesized as described in our earlier publication.⁴ The molecular weight of the polymer was 95 kDa as determined by gel permeation chromatography (GPC)

using dimethylformamide as solvent. The column was calibrated using polystyrene standards. Fibers were extruded from the polymer powder using a microextruder (Randcastle, Cedar Grove, NJ) at 135°C using a 1 mm die. The fibers were drawn 2.5X at 55°C to a final diameter of 90 – 100 µm on a draw frame. All the three samples, the as-polymerized powder, the undrawn fiber and the drawn fiber were analyzed.

DSC scans were obtained using a Mettler 823e DSC equipment (Mettler Toledo, Columbus, Ohio). The samples were sealed in an aluminum pan and the scans during the heat-cool-reheat cycles at 10°C/ min were recorded.

Melt rheology data were obtained using Malvern RH2000 capillary rheometer with 0.5 mm die.

Structural investigations were carried out by X-ray diffraction (XRD). Combined WAXS, MAXS and SAXS data were collected at the Argonne Photon Source (APS) on the DND-CAT beam line 5ID-D at a wavelength (λ) 0.7293 Å using three detectors at distances of 199.9 (WAXS), 1014.0 (MAXS) and 7500.0 mm (SAXS) covering three overlapping q -ranges: SAXS - 0.01 to 0.15 Å⁻¹ (600 to 50 Å); MAXS - 0.12 to 0.6 Å⁻¹ (50 to 10 Å) WAXS: - 0.6 to 2.5 Å⁻¹ (10 to 2.5 Å); values in parenthesis are the Bragg spacings (d -spacings) corresponding to the q values (scattering vector $q = (4\pi \sin\theta)/\lambda = 2\pi/d$). The samples were hermetically sealed aluminum DSC pans (TA-Instruments). The X-ray data were recorded as the samples were heated at 10°C/min.

Empty pan scattering, recorded before each class of samples (powder, drawn and undrawn fibers), was subtracted from the data with the samples in the pan. Intense, sharp WAXS aluminum peaks from the pan, which are at q values higher than those of the diffraction peaks of interest in this study, were not an issue during this subtraction. Aluminum scattering from the pan was negligible in MAXS and SAXS data.

Lorentz corrections could not be made because the fibers, which were squished in the aluminum pan, were neither random nor aligned and their orientation changed during heating. Ignoring this correction does not alter the discussions that are based on the positions and the presence or absence of the various peaks. Since the Lorentz factor will affect the peak areas, and because the integrations were carried out over a limited angular range, the values reported here for crystallinity are not absolute but are only a relative indication of the level of the crystallinity.

1-D radial X-ray scans obtained from azimuthal averaging the 2D images were profile-fitted using OriginR software (OriginLab, Northampton, MA). This averaging minimizes the effect of the differences in the orientations of the ordered and the disordered phases in the crystallinity values. Lorentzian profile was found to best reproduce the shape of peaks in all of the WAXS, MAXS and SAXS scans. These scans were analyzed in detailed to derive structural parameters (d -spacings, crystallinity and crystallite size) that were used to interpret the nature of the thermal transitions observed in the DSC scans.

RESULTS

DSC scans obtained from various samples (Figure 2) show that there are numerous thermal transition during first heating segment that are highly dependent on the state of the starting material. These transitions offer a clue to the molecular organization and the liquid crystalline nature of the polymer. Temperature-resolved X-ray diffraction measurements were carried out to examine the structural organization of the polymer chains in the various phases between these transitions during the heating cycle, and explain the rheological behavior.

DSC results

Representative DSC scans of samples with different thermal and mechanical histories (as-polymerized powder, undrawn fiber, drawn fiber, re-heated samples) are plotted in Figure 2. Since the process history gets erased upon melting the polymer, the scan during cooling and re-heating were the same for all three types of samples, and hence is shown only for the drawn fiber. The samples show a melting point (T_m) of 50°C in the powder and undrawn fibers and at 55°C in the drawn fibers. Consistent with previous reports, no glass transition temperature (T_g) was observed in any of the samples (powder, fiber and drawn fiber) in the temperature range used.²⁴ Given the low melting point of the polymer, it is possible that poly(DTD DD) melts soon after the onset of local relaxations that would have triggered a T_g . Irrespective of the starting material, there was a single crystallization peak at 40°C in the scan obtained during the cooling segment of the heat-cool-reheat cycle.²³ During the first heat, the temperature of the various transitions, the amount of heat flow (peak intensity) and the rate of transformation (width of the peak) vary with the structure (processing history) of the sample. The melting peak in the as-polymerized powder is broader than in the undrawn and drawn fibers. Drawing the fiber raises the melting temperature and makes the melting peak narrower, a signature of the expected enhancement of the molecular order. During the heating cycle, along with the main melting transition, there are additional minor transitions (Table 1). In the following sections we will focus on structural changes at different length scales that occur during these transitions by using WAXS, MAXS and SAXS data.

X-ray scattering data

Data obtained using separate detectors simultaneously for each of the three angular ranges (SAXS, MAXS and WAXS) at each temperature from ambient to the complete melting of the polymer permits unambiguous interpretation of the thermally induced structural changes at molecular and fibrillar length scales. Examples of these data from a drawn fiber are shown in Figure 3. Similar data were obtained from powders and undrawn fibers (Supplementary Figures S1 and S2, respectively). These data are average of five sequential images at each temperature that were collected to monitor radiation damage and other artifacts; none were detected. These scans were resolved into their constituent peaks to determine the various aspects of the structure. Examples of profile analyses in each of the three q -ranges are shown in Figure 4.

Wide-angle scattering (Figures 3 and 4a): The WAXS profile could be resolved in two peaks.²⁶ In the 29°C scan, there is a sharp equatorial peak at $q=1.43 \text{ \AA}^{-1}$ ($d=4.39 \text{ \AA}$)

and a broad halo at $q = 1.42 \text{ \AA}^{-1}$ ($d = 4.42 \text{ \AA}$). The sharp peak arises from an ordered structure, and the broad halo from a disordered phase. This diffuse halo dominates the scattering at higher temperatures. The fraction of ordered component (X_c) was calculated from the intensity (peak area) ratio of the sharp peak to the total scattered intensity. The changes in the X_c and the d -spacing (d) of these two phases with temperature are plotted in Figure 5.

Medium-angle scattering (Figures 3 and 4b): A single sharp meridional peak ($q = 0.22 \text{ \AA}^{-1}$, $d = 28.5 \text{ \AA}$) is present at low temperatures ($T < 60^\circ\text{C}$). As the temperature is increased, the peak shifts to lower angles, and at $T > 60^\circ\text{C}$ a new broader peak appears at higher angles ($q = 0.275 \text{ \AA}^{-1}$; $d = 22.8 \text{ \AA}$), again along the meridian. These sharp and the broad peaks coexist at intermediate temperatures. The changes in the features of this scattering with temperature are shown in Figure 6a as changes in their d -spacings and in Figure 6b in the form of the changes the intensities of the two peaks.

Small-angle scattering (Figures 3 and 4c): In SAXS data, a broad equatorial peak at $q = 0.089 \text{ \AA}^{-1}$ ($d = 70.6 \text{ \AA}$) is present at lower temperatures ($T < 60^\circ\text{C}$), and upon further heating ($60 < T < 90^\circ\text{C}$), this peak is replaced by a broader peak at lower angles. No SAXS peak is observed at higher temperatures. Such equatorial scattering has been observed in other polymers with fibrillar structures.^{27–29} An additional low-angle diffuse scattering was used to obtain proper profile fitting.^{30, 31} The peak intensities and the d -spacings of the two peaks derived from the profile analysis at each of the temperatures are plotted as a function of temperature in Figure 7.³⁰

DISCUSSION

The structural transitions seen in the polymer can be discussed in terms of systematic changes in the packing of the chains. This local order arises primarily from the hydrophobic interactions: the main chain has hydrophobic moieties between the amide and ester functionalities, and the side chain is completely hydrophobic. In addition, structural order is also imposed by the intermolecular hydrogen bonding, and the packing of molecules of asymmetric shapes.^{32, 33} These interactions in poly(ester-amide)s give rise to ordered clusters with layered structure that persists in the melt indicating the presence of a liquid crystalline structures.³⁴

Structural model

On the basis of the X-ray scattering data from a large variety of samples, we propose the structural organization for the polymer shown in Figure 8. This organization accounts for the key meridional and equatorial reflections in the drawn fiber at room temperature. The structure is driven by the bending of the side chain, and the interchain interactions through the hydrogen bonding between ester and amide groups. The model depicts the essential features structure at several length scales. The intra-chain structure depicts the molecular conformation in a single chain. At a larger length scale, there is another intra-chain feature in the form of $28.5 \text{ \AA}$ separation of the side chains along the chain axis, as indicated by the meridional MAXS peak at $q = 0.22 \text{ \AA}^{-1}$. This separation is also the distance between two

monomers or amide linkages along the chain-axis.²² The model shows the packing of the chains with a lateral spacing of 4.4 Å between the chains corresponding to the equatorial WAXS peak at $q = 1.43 \text{ Å}^{-1}$. At a larger length scale, there is another lateral structure that arises from the organized packing of the polymer chains into coherently scattering bundles resulting in a fibrillar structure with a 71 Å spacing between the fibrils, as indicated by the equatorial SAXS peak at $q = 0.089 \text{ Å}^{-1}$.

Other members in the family of poly(ester amides), obtained by changing the number R of methylene groups of the alkyl pendant chain, and the number Y of the methylene groups in the aliphatic diacid (main chain) (Figure 1) have been discussed in previous publications.^{4, 22, 24, 25} These polymers are abbreviated as poly(R,Y). In this notation, the polymer studied here is poly(12,10). All of these polymer show the same lateral chain spacing of ~ 4 Å. However, while poly(2,2) and poly(2,10) are amorphous, poly(8,8) and poly(12,10) are semicrystalline. Both poly(8,8) and poly(12,10) show a chain-axis repeat of 27.6 Å. But, unlike poly(12,10), poly(8,8) does not crystallize upon cooling, and consequently does not melt during the re-heat cycle, indicating its far slower crystallization kinetics. Amorphous nature of poly((2,10) and similarities between poly(8,8) and poly(12,10) suggest that long pendant chain and long diacid chain are both prerequisites to obtain the mesophase behavior observed in poly(12,10).

In the model, the alkyl/alkyl ester side chain lies alongside the main chain. This is the most favorable configuration for at least three reasons. First, the hydrophobicity of both the pendent chains and the backbone determine this mode of packing. Second because of the absence of steric hindrance between the side chain and the amide moiety, the alkyl groups on the pendant side chain are able to bend so as to be parallel to the main chain. Third, because of the low energy for rotation about the C-O-C bonds in the ester group, the side-chain is able to rotate more freely to orient itself along the main-chain axis. The separation of the hydrophilic and the hydrophobic moieties (amide and ester groups) was found to induce hexagonal columnar structure^{24, 35} in biforked³⁶ macromolecules with flexible side chains.

A space-filling model of the proposed structure for poly(12,10) is shown in Figure 8b in which the seven chains are packed in a hexagonal of side 4.4 Å. The three side chains disposed at 120° form a repeating structure along the chain-axis. The model was built in such a way as to avoid unfavorable steric interactions. Conformational study was carried out on this structure using Schrödinger-Material Science Suite³⁷ using prebuilt OPLS force field.³⁸ Heating-cooling cycles on the initial conformation shown in Figure 8b resulted in a final configuration that preserved the global conformation (columnar hexagonal). Furthermore, the side chains retained their orientation along the main chain. Inter-chain interactions seem to take place through hydrogen bonding between the ester and the amide groups (Figure 8c). This is confirmed by the IR data discussed below.

The packing of the chains is driven by two factors: the separation of the hydrophilic and hydrophobic moieties, and the hydrogen bonding. The presence of both amide and ester groups in poly(DTD DD) favors the hydrogen bonding between the chains. Hydrogen bonding occurs between donor O-H or N-H groups and acceptor N, O-C or O-H groups. Infrared spectra obtained by Jaffe et al.²² indicate the presence of three types of amide group

configurations: free unbonded (1680 cm^{-1}), disordered hydrogen bonded (1652 cm^{-1}) and ordered hydrogen bonded (1644 cm^{-1}). Above 40°C , the population of ordered hydrogen bonded amide decreases sharply relative to that of the other two types. This suggests that the amide groups are strongly hydrogen bonded at room temperature. This is further confirmed by the increase in the intensity of the 3300 cm^{-1} band as the polymer was cooled from 43 to 39°C , indicating more numerous hydrogen bonds between N-H and the amide carbonyls. Jaffe et al. also found that the intensity of the 3380 cm^{-1} band corresponding to N-H bonded to ester carbonyl remains unchanged. This was explained by suggesting that the hydrogen bonded esters are associated with the amorphous or the disordered H-bonds. The ester bonds adapt different conformations depending on whether they are on the main (1759 cm^{-1}) or the side chain (1740 cm^{-1}). Upon cooling from high to room temperature, the two bands shift to lower frequencies (1752 and 1730 cm^{-1}). Thus, there are two sets of ester bands, 1759 and 1740 cm^{-1} in the disordered phase, and 1752 and 1730 cm^{-1} in the ordered phase.²² These IR results show that both the amide and ester groups participate in hydrogen bonding, and at lower temperatures they are present in a structurally ordered environment of the close packed chains at room temperature.

Liquid crystalline phases

The hydrogen bonding between the different hydrogen donors and acceptors in the polymer occurs in a single plane, and the spacing between these planes at room temperature is same as the length of the monomeric unit, $28.5\text{ \AA}$. The three-fold rotation imposed by the pendant chain, and the strong hydrogen bonding leads us to propose the layered structure shown in Figure 9a. The sharp peaks in the WAXS and MAXS scans, and the endotherm and exotherm in the DSC scan might suggest that the polymer is crystalline at room temperature. However, in the 2D diffraction patterns of the oriented samples, there is a single $4.5\text{ \AA}$ equatorial reflection in the WAXS scan; the rotational disorder induced by the weakly interacting hydrophobic segments prevent the formation of a highly ordered 3D crystalline structure. This is substantiated by the MAXS peaks that are purely meridional, and by the conspicuous absence of any off-axes reflections. The presence of a highly ordered layer structure, and similarities with the diffraction patterns from other mesogenic polymers,⁸ clearly indicates that the room temperature structure is liquid crystalline.²³ Based on the proposed bond orientational order of the interchain hydrogen bonds and the d -spacing being equal to the length of the monomeric unit, we attribute the diffraction pattern at room temperature to a hexatic smectic B (SmB) phase.³⁹

As the polymer is heated, at least three exothermic transitions can be identified in the DSC scans (Figure 2 and Table 1). In addition to the main melting peak, the scans of the fibers show a minor transition before melting and another minor transition after melting. These transitions occur as the polymer transforms into progressively less ordered structures with increase in temperature. The different structures between these transitions can be identified by examining the MAXS data plotted in Figure 6b in the form of the d -spacing of the meridional peak as a function of temperature alongside the DSC scan, also reproduced in the figure. It can be seen that the d -spacing decreases in discrete steps from $28.5\text{ \AA}$ below 40°C to 27.7 near the melting transition at 60°C , and then to $24.1\text{ \AA}$ in the melt. The d -spacings observed in various temperature regimes are shown in Table 1. Such temperature dependent

changes are also apparent in the MAXS and SAXS intensities (Figures 6a and 7), and somewhat less distinctly in WAXS data (Figure 5). These systematic changes were observed reproducibly in several different samples with different processing histories.

Between 40 and 60°C, small, molecular-scale reorganization in the structure leads to orientational and positional disorder as indicated by the changes in the peak position, and the broadening and weakening of all the peaks arising from the ordered phase (Figures 5–7). The small decrease in the layer *d*-spacing from 28.5 to 27.7 Å at 44°C is likely due to a tilt of the molecules with respect to the layer normal, and hence suggests the transition to hexatic smectic F (SmF) phase.

The *d*-spacing of the SmF phase continues to decrease to 25.7 Å at higher temperatures. At ~ 60°C, we speculate that the hexatic phase with both rotational and positional order changes to a smectic phase with only positional order, smectic C (SmC).⁴⁰ This is indicated by a large decrease in the layer *d*-spacing to 23 Å. The smectic F and smectic C phases coexist between 65 and 85°C.⁴¹

Even though the main melting event occurs at 60°C, the polymer is not sufficiently molten to flow until about 120°C as determined by capillary rheometer data. Although the polymer is disordered at 80°C as seen in the WAXS data, there is some local order as determined by the broad meridional peak in MAXS. Minor structural changes continue to occur between 80 and 100°C as indicated by the transitions in the DSC and X-ray scattering data. The rigidity of the main chain that allows the polymer to maintain a semblance of the 2D smectic order in the melt contributes to the observed low melt viscosity of the polymer.

In summary, as the temperature increases the polymer goes through the following phases: SmB→SmF→SmC→Melt (Figure 8f). Following the general rule that small structural changes show transition enthalpies smaller than those with large structural changes, the transition enthalpies between smectic phases with order within the layers is expected to be small (SmB- SmF) and those between smectic phases with and without order within the layers (SmF – SmC) to be significantly higher.⁴²

The exotherm during heating and the endotherm during cooling were highly reproducible upon repeated heat-cool cycles between –20 and 140°C.²³ However, lowering the maximum temperature in increments of 10°C to 70°C resulted in gradual attenuation of the exothermic and endothermic peaks upon successive heat-cool cycles. No such attenuation observed when the maximum temperature was above ~ 100°C. The peak intensities revert to the original values when the sample is allowed to sit for 24 h at room temperature. We also observed similar phenomenon. This complex behavior can be explained in view of the structural transformation discussed here. Although the main melting peak is at 60°C, there are minor transitions at temperatures between 60 and 100°C, and the polymer is completely molten at temperatures above 120°C. Thus, when the polymer is cooled at temperatures between 70 and 100°C, it is possible that the unmelted crystalline domains act as defects to inhibit crystallization. This reduces the exothermic peak during cooling and the subsequent exothermic peak upon heating. However, upon aging at RT, the metastable phases slowly transform to the initial stable phase, and thus the initial endothermic and exothermic

transitions are recovered. The structural features of the different phases between the various thermal transitions will be elaborated below.

Structural transitions

Hexatic smectic B phase (< 40°C): At temperatures below the first endothermic peak (40°C), in the solid state, the WAXS patterns show a sharp peak overlaid on a diffuse halo (Figure 4a). This shows that the presence of both ordered and disordered phases in the polymer. These d -spacings of the two peaks calculated from their positions correspond to the nearest neighbor separation between the chain segments. This inter-chain distance is 4.39 Å in the ordered phase and is smaller than the 4.42 Å in the disordered phase; this difference that is outside the errors in the measurement. Below 40°C, the d -spacings of the ordered and the disordered peak increase from 4.38 to 4.40 Å and 4.41 to 4.43 Å, respectively; the thermal expansion coefficients for the ordered and the disordered phases are about the same, $\sim 3 \cdot 10^{-4} \text{ K}^{-1}$. The results of the profile analysis of these scans show that the crystallinity remains unchanged at about 30% below 40°C, and then gradually decreases to zero above 40°C (Figure 5).

In the MAXS data, there are both a sharp peak and a broad halo. The broad halo is weak at these temperatures (Figures 3, 4b and 6a). The position of the sharp peak ($q = 0.22 \text{ Å}^{-1}$, $d = 28.5 \text{ Å}$) remains essentially unchanged in this temperature range (Figure 6b).

In the SAXS scans, the presence of a broad equatorial reflection at $q = 0.089 \text{ Å}^{-1}$ (Figure 3) suggests that the polymer chains assemble not into a crystallites of varying sizes often seen in semicrystalline polymers, but into fibrils of a definite size so as to give rise a well-defined average spacing of 71 Å between the fibrils.

Hexatic Smectic F phase (40 < T < 60°C): DSC scans show a small endothermic transition just after 40°C, and before the major melting transition at 60°C (Figure 2). Analysis of the WAXS data shows that as the crystallinity begins to decrease in this temperature range, the d -spacing increases at a faster rate than that below 40°C (Figure 5): the thermal expansion coefficients for the ordered and the disordered phases, respectively, are $7.7 \cdot 10^{-4}$ and $9.5 \cdot 10^{-4} \text{ K}^{-1}$ compared to $\sim 3 \cdot 10^{-4} \text{ K}^{-1}$ below 40°C. The disordered phase, as expected, shows a larger thermal expansion than the ordered hexatic phase above 40°C

In MAXS, the data in Figures 3 and 6 show that the sharp peak at $q = 0.220 \text{ Å}^{-1}$ ($d = 28.5 \text{ Å}$) becomes broader, weaker, and shifts to higher q values ($q = 0.228 \text{ Å}^{-1}$; $d = 27.5 \text{ Å}$).

In the SAXS scans (Figure 3), the 71 Å fibrillar peak becomes weaker, and a new equatorial peak appears at a lower angle ($d = 150 \text{ Å}$), and its intensity increases indicating the appearance of a new organization of the polymer chains (Figure 7).

In summary, all the three segments of the X-ray data continue to show the features present at lower temperatures across this minor thermal transition, but there are changes that are indicative of the onset of structural disorder prior to melting at 60°C. The reflections from the smectic phase in the SAXS and MAXS scans are weak and diffuse compared to that

from the hexatic phase. This could be because the order is limited to 3 or 4 units, and the small contrast between the smectic component and the matrix.

Smectic C phase ($60 < T < 80^{\circ}\text{C}$): The DSC, WAXS and SAXS data in this temperature range capture the melting of the hexatic ordered structure. In this temperature range, the DSC scans of the drawn fibers show a major endothermic peak at 60°C arising from the primary melting transition in the polymer. In fact, the ordered fraction, as seen in the WAXS data (Figures 3 and 5), disappears confirming that melting has occurred. During this transition, the ordered structure begins to disappear at $\sim 70^{\circ}\text{C}$ as indicated by the decrease in crystallinity (relative increase in the intensity of the amorphous halo), and the d -spacing of the hexatic peak increases and approaches that of the amorphous halo (Figure 5).

At larger length scales, the MAXS data show the coexistence of two peaks as seen in Figure 3 (data recorded at 70°C). A new broad MAXS peak appears at higher q value $q=0.275\text{ \AA}^{-1}$ ($d=22.8\text{ \AA}$), along with the pre-existing sharp peak ($q=0.226\text{ \AA}^{-1}$, $d=27.7\text{ \AA}$). As can be seen in Figure 6, as the d -spacings of both the MAXS peaks decrease rapidly, the intensity of the broad peak remains higher than that of the sharp peak. This meridional peak suggests the presence of layered structure, and the diffuse WAXS peak suggests that there is little lateral order in the organization of the polymer stems within the layer. The diffraction features observed in this temperature are reminiscent of the smectic LC phase.^{8, 43}

In the SAXS, the intensity of the low temperature fibrillar peak ($71\text{ \AA}$; designated as LT peak in Figure 7) decreases continuously as the hexatic structure melts. Meanwhile, the intensity of the high temperature fibrillar peak ($150\text{ \AA}$; designated as the HT peak in Figure 7) increases and then decreases.

Premelting transitions between 80 and 100°C : The polymer appears to be disordered above 80°C as evidenced by the absence of any hexatic features in the WAXS scans, but there is evidence some order as seen in the broad peak in MAXS (Figure 3). The sharp peak at $q=0.25\text{ \AA}^{-1}$ ($d=25.6\text{ \AA}$) is very weak, while the broad peak at $q=0.31\text{ \AA}^{-1}$ ($d=20.3\text{ \AA}$) remains intense. Coexistence of the remnants of an ordered hexatic phase and a disordered disordered phase is not unexpected.²²

Molten phase ($T > 100^{\circ}\text{C}$): Above 100°C , the polymer is completely molten, and there are no thermal transitions in the DSC scans. Absence of any SAXS peak confirms that there are no residual fibrillar structure. In this temperature range, the sharp MAXS peak disappears, but the broad MAXS peak at $q=0.31\text{ \AA}^{-1}$ ($d=20.3\text{ \AA}$) remains suggesting the persistence of stacked layers of monomeric units molecularly ordered in the axial direction even though material is molten. This, combined with the equatorial diffraction halos at $d \sim 5\text{ \AA}$ (WAXS) corresponding to the lateral separation of the polymer chains, shows that local 2D order is still present. This persistence of 2D-order in the melt is suggestive of the smectic-like ordering in a thermotropic liquid crystalline polymer. The meridional layer line reflection seen at the highest temperature we have investigated (130°C) suggests that we have a 2D-LC order. However, the large width of this reflection suggests that this ordering is limited to $\sim 41\text{ \AA}$ (at 116°C) nm, and hence is not expected to show any optical birefringence.²³

Melt Rheology

The proposed structure can be used to explain the observed rheological behavior of the polymer in terms of its liquid crystalline characteristics. Melt viscosity data obtained from capillary rheometry (Figure 9) shows that the melt viscosity is two orders of magnitude lower value for an equivalent molten entangled polymer. Given the molecular weight of the studied polymers (95 KDa), the melt viscosity for an entangled melt polymer according to Fox-Flory power law ($\eta_0 \propto M^{3.4}$), would be $\sim 6.3 \cdot 10^6$ Pa. s. However we noticed a much lower viscosity ($\sim 2.5 \cdot 10^3$ Pa/s at 115°C). The lower viscosity is typically attributed to low chain entanglement expected in low molecular weight polymers.⁴⁴ But because the polymer used in this study has a rather high molecular weight (100 KDa), the low viscosity is most likely due to the liquid crystal behavior as suggested by the thermal and X-ray scattering results. The 2D order in the melt may arise from the possible ordered hydrogen bonded ester and amide groups. The persistent 2D order could inhibit chain entanglement in the melt which in turn lead to low viscosity.

We noticed that melt properties of the polymer does not change significantly upon extrusion, and can be re-extruded using similar processing conditions. In fact, the molecular weight of the polymer remains the same after being processed at 135°C. However, the polymer decreases considerably *in vivo* showing that polymer degrades when surrounded by biological tissue.¹⁹

CONCLUSIONS

Thermotropic liquid crystalline behavior in an aromatic polyester(amide), poly(DTD DD) was investigated by detailed analysis of x-ray scattering data at three length scales using small-, medium- and wide-angle scattering obtained simultaneously with DSC scans. The data enabled us to model the structure and interpret the thermal transitions observed in the DSC scans.

1. The packing of the polymer chains is driven mostly by the hydrogen bonding in the amide and ester carbonyl groups. The side chains are packed along the backbone chain with a chain-axis repeat of 28.5 Å.
2. The hexatic structure observed under ambient conditions melts to form a smectic liquid crystalline structure at a 60°C, and eventually melt into an isotropic fluid that flows at 120°C.
3. X-ray scattering results indicate that a 2D order is present even in the melt. The amide linkages are separated by 20 Å along the chain axis, and the chains are laterally separated by 4.7 Å.
4. The alignment of the rigid segments into a well-defined cluster gives rise to the fibrillar structure in which the fibrillar bundles of polymer chains are separated by 70 Å. In the smectic phase, these bundles merge to form smectic layers with a domain size of ~ 150 Å.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Chemical structure of poly(desaminotyrosyl-tyrosine dodecyl dodecandioate), poly(DTD DD). Chemical Formula: $C_{42}H_{61}NO_7$. Exact Mass: 691.44 Da. Molecular weight: 691.95 Da. Elemental analysis: C - 72.90; H - 8.89; N - 2.02; O - 16.19.

Figure 2.

DSC scan of poly(DTD-DD) samples. Data during heating for as-polymerized powder, undrawn and drawn fibers are shown in the figure. Cooling and re-heat scans were similar for all the samples, and hence only the set from the drawn fiber is shown.

Figure 3.

X-ray diffraction data from a drawn fiber at several temperatures to highlight the structural transitions. The inset show one of the 2D diffraction patterns from the fiber. The curves have been offset vertically for clarity.

Figure 4. Profile analysis of the XRD scans illustrated using the data from a drawn fiber. The components are shown, and the sum of the components is overlaid on the observed data, which are shown as points. (a) WAXS data at 30°C. (b) MAXS data at 70°C. (c) SAXS data at 60°C.

Figure 5.

Results from the analysis of the WAXS scans of the drawn fiber. Changes in (a) crystallinity and (b) *d*-spacing with temperature. Lines are drawn free-hand through the data points to emphasize the transitions. The DSC trace is from Figure 2.

Figure 6.

Results from the analysis of the MAXS scans of the drawn fiber. Changes in (a) d -spacings and (b) peak intensities with temperature. Lines are drawn free-hand through the data points to highlight the transitions. The DSC trace is from Figure 2.

Figure 7.

Results from the analysis of the SAXS scans of the drawn fiber. Changes in (a) d -spacings and (b) intensity of the low- and high-temperature peaks. Lines are drawn free-hand through the data points to highlight the transitions. The DSC trace is from Figure 2.

Figure 8.

Structural model for the polymer: (a) Schematic representation of the polymer chain identifying the d-spacings corresponding to the MAXS peak (28.5 Å). The side chains (shown in red, blue and green in cross section) are disposed at 120° around the main chain (open circle). (b) Hexagonal packing of the polymer chains shown in cross section, using the color scheme in Figure (a) (left) and using space-filling model (right). (c) Longitudinal view of the chains using space-filling model. (d) Illustration of the local chain conformation and inter-chain interactions. (e) Packing of the chains into fibrils. (f) Depiction of the packing of the stems into hexatic array at room temperature that transform into smectic layers, and then into an isotropic melt upon heating.

Figure 9. Shear viscosity shown as a function of shear rate in poly(DTD-DD) at different temperatures.

Summary of the d -spacings ($\text{\AA}$) observed between various thermal transitions observed in poly(DTD DD) during heating. The temperature ranges depend on the processing conditions as seen from Figure 2. The values shown are from the dawn fibers.

Table 1

q -range and the spatial features	Temperature ($^{\circ}\text{C}$) $\rightarrow$	< 45	45 to 65	65 to 85	85 to 100	> 100
	Phase designation	Smectic B	Smectic F	Smectic F $\rightarrow$ Smectic C	Smectic C	Ordered Melt
WAXS (0.01 to 0.15 $\text{\AA}^{-1}$) Lateral chain spacing	Ordered	4.39	4.45	4.5		
	Disordered	4.42	4.5	4.6	4.65	4.7
MAXS (0.12 to 0.6 $\text{\AA}^{-1}$) Meridional monomer spacing	Ordered	28.5	28.5 to 27.7			
	Intermediate			27.7 to 25.7		
	Disordered			23 to 20	20	20
SAXS (0.6 to 2.5 $\text{\AA}^{-1}$) Fibril diameter	Ordered	71	71			
	Intermediate			150	150	
Transition temperature ($^{\circ}\text{C}$) $\rightarrow$			43	61.8	88.5	
Transition enthalpy (J/g) $\rightarrow$			2.36	18.34	2.20	