Peptoid Oligomers with α-Chiral, Aromatic Side Chains: Effects of Chain Length on Secondary Structure

Cindy W. Wu, Tracy J. Sanborn, Ronald N. Zuckermann, and Annelise E. Barron

Abstract: Oligomeric N-substituted glycines or “peptoids” with α-chiral, aromatic side chains can adopt stable helices in organic or aqueous solution, despite their lack of backbone chirality and their inability to form intrachain hydrogen bonds. Helical ordering appears to be stabilized by avoidance of steric clash as well as by electrostatic repulsion between backbone carbonyls and π clouds of aromatic rings in the side chains. Interestingly, these peptoid helices exhibit intense circular dichroism (CD) spectra that closely resemble those of peptide α-helices. Here, we have utilized CD to systematically study the effects of oligomer length, concentration, and temperature on the chiral secondary structure of organosoluble peptoid homooligomers ranging from 3 to 20 (R)-N-(1-phenylethyl)glycine (Nppe) monomers in length. We find that a striking evolution in CD spectral features occurs for Nppe oligomers between 4 and 12 residues in length, which we attribute to a chain length-dependent population of alternate structured conformers having cis versus trans amide bonds. No significant changes are observed in CD spectra of oligomers between 13 and 20 monomers in length, suggesting a minimal chain length of about 13 residues for the formation of stable poly(Nppe) helices. Moreover, no dependence of circular dichroism on concentration is observed for an Nppe hexamer, providing evidence that these helices remain monomeric in solution. In light of these new data, we discuss chain length-related factors that stabilize organosoluble peptoid helices of this class, which are important for the design of helical, biomimetic peptoids sharing this structural motif.

Introduction

Biological polymers such as DNA, RNA, and polypeptides have evolved to perform a myriad of interdependent structural and catalytic functions that together enable cellular life. These polymer systems are unique in their ability to fold and self-assemble into complex and specific structures. Inspired by natural polymer systems, organic and medicinal chemists have worked to develop non-natural oligomer systems that mimic some of the fundamental molecular features of proteins and DNA. Various groups have ventured into bioinspired molecular design to create novel oligomer scaffolds such as peptoids,1,2 vinylogous polypeptides,3 peptide nucleic acids,4 oligoureas,5 oligopyrrolinones,6 β-peptides,7 and γ-peptides.8 Others have created novel oligomers that include stiff, aromatic groups in the backbone that cause them to fold or pleat into ordered structures in polar solvents, including the oligo(phenylene ethynlenes)9 and aedamers.10 Non-natural oligomers generally are resistant to enzymatic degradation, increasing their potential for in vivo stability as therapeutics or as biomaterials. The development of a man-made polymer system that captures the defining characteristics of natural polypeptides, including sequence and length specificity and the ability to fold into defined structures, will not doubt offer intriguing avenues for design of novel therapeutics and for the engineering of bio-compatible, nanostructured materials.11,12 Fundamental studies of the folding propensities of novel, sequence-specific oligomers may also provide us with deeper insight into protein folding by better revealing the hierarchies of forces that enable mimicry of the natural protein paradigm, in which function derives from folded structure, and folded structure is derived from heteropolymer sequence.

Poly-N-substituted glycines or “peptoids” are a unique class of non-natural, sequence- and length-controlled polymers that...
are based on a polypeptide backbone. They differ in that the side chains are appended to the amide nitrogen rather than to the α-carbon (see top of Table 1). Like polypeptides, peptoids are accessible by automated, solid-phase synthesis. As candidate peptide mimics, peptoids offer the advantages of protease-resistance,15,16 biocompatibility,16 facile incorporation of diverse side chain chemistries through a “submonomer” synthetic protocol,2 and generally high monomer coupling efficiencies that enable robotic synthesis of long chains (up to ~50mers).17,18 Additionally, proteinogenic side chains and/or their close mimics can be incorporated into peptoids to create biomimetic oligomers.15,19

In previous work, we have shown that a variety of simple peptoid oligomers exhibit intense CD spectra that are indicative of the presence of regularly repeating secondary structure, and furthermore that are strongly reminiscent of the CD spectra of peptide α-helices.17 As was shown for helical polysaccharides,20 the handedness of peptoid helices, which have no chiral information in the backbone, can be dictated by the handedness of α-chiral side chains.17 For a variety of oligomers in this class ranging from 12 to 30 residues in length, “α-helix-like” CD spectra were observed in both organic and aqueous solution, where solvent compatibility was dependent upon both side chain chemistries and oligomer composition.17

Given the evident promise of peptoid oligomers as a new class of protease-resistant, biocompatible peptide mimics, we seek to better understand their conformational preferences in solution. Of particular interest to us for further studies are peptoids with organic and aqueous solution. Of particular interest to us for seeking to better understand their conformational preferences in solution, we seek to further investigate the CD spectra of peptoid oligomers comprised of α-chiral, aromatic side chains and determined the effects of chain length, concentration, and temperature on their secondary structures, as monitored by CD. For peptoid oligomers shorter than 11 residues, we see strong evidence of a low free energy barrier for interconversion between peptoid structures with cis and trans amide bonds, previously predicted by modeling21 and observed in 2D-NMR structural studies of a peptoid oligomer with this class of side chains.22

### Materials and Methods

**Peptoid Synthesis and Purification.** Peptoids were synthesized on 0.1 mmol of PEGA Rink amide resin (NovaBiochem, San Diego, CA) at a typical substitution level of 0.45 mmol/g. Fully automated synthesis was accomplished on a PE Biosystems 433A Peptide Synthesizer (Foster City, CA) with software protocols written in-house, using the methodology developed by Zuckermann et al.2,17 The oligopeptoid was cleaved from the resin with a solution of 95% trifluoroacetic acid (TFA) and 5% water, frozen at ~85 °C, and subsequently lyophilized on a Labconco freeze-drying system.

Peptoid oligomers were analyzed by reversed-phase HPLC on a C4 column (Vydac, 5 μm, 300 Å, 3.2 × 250 mm) with a Waters Alliance 2690 separations module, and detected by UV absorbance at 220 nm with a Waters Dual λ 2487 detector. Data were analyzed with Waters Millenium software. All separations were run at a column temperature of 60 °C. For analytical RP-HPLC separations, a linear gradient of 20–95% solvent B in solvent A over 50 min was employed at a flow rate of 0.5 mL/min. Here, solvent A = 0.1% TFA in water, and solvent B = 0.1% TFA in acetonitrile (oligomers 1–12) or 0.1% TFA in 2-propanol (oligomers 13–20). Preparative HPLC was performed on a Rainin system (Varian Chromatography Systems, Woburn, MA) with a Vydac C4 column (15 μm, 300 Å, 10 × 250 mm) at a flow rate of 8 mL/min, with the same solvent gradient as for analytical separations.

Electrospray mass spectrometry of synthesis products to confirm correct molar mass and high purity was performed either at Northwestern University’s Analytical Chemistry Facility or at the University of Illinois, Urbana-Champaign Mass Spectroscopy Facility.

**Amine Submonomers Used in Peptoid Synthesis.** (R or S)-N-(1-phenylethyl)glycine (Arpe or Npe) and N-(1-phenylmethyl)glycine (Npm) monomers were made from the amines (R or S)-1-phenylethylamine and phenylmethylamine, respectively, which were obtained from Aldrich Chemical Co. (Milwaukee, WI) at a purity >99%. Structures of the peptoid side chains derived from these amine submonomers are shown in Table 1.

**Circular Dichroism (CD).** CD measurements were performed on a Jasco model 715 spectropolarimeter (Easton, MD). Stock solutions (~2 mg/mL) for dilution to appropriate concentrations for CD were made immediately before analysis in tared 2.0 mL vials by precise weighing of added solvent and at least 2 mg of lyophilized peptoid powder, to produce a sample of accurately known concentration. The stock solution was then diluted to CD sample concentration (typically ~60 μM), again by careful weighing of the solution and solvent added to a tared microvial.

CD spectra were acquired in a quartz cylindrical cell (Hellma model 121-QS, Forest Hills, NY) with a path length of 0.02 cm, employing a scan rate of 100 nm/min. CD spectra reported here represent the average of 40 successive spectral accumulations. For temperature-dependence studies, a water-jacketed CD sample cell with a path length of 0.02 cm was used (Hellma model 165-QS) and temperature was controlled with a Jasco 505A temperature controller.

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Table 2. Peptoid Homo-Oligomer Structures, Mass Confirmation, and Purity

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<th>monomer sequence (amino-to-carboxy)</th>
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<th>purity, %</th>
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* As estimated by analytical reversed-phase HPLC of crude product. All compounds were purified to >97% homogeneity before analysis by CD.

controlled with an external water bath (Model RTE-111, Neslab, Portsmouth, NH). In the concentration study, for peptoid samples having concentrations lower than 20 mM, a square quartz CD cell with a path length of 1 cm was used (Hellma model 114B-QS). Data are expressed in terms of per-residue molar ellipticity (deg cm²/dmol), as calculated per mole of amide groups present and normalized by the molar concentration of peptoid.

Results and Discussion

Synthesis and Characterization of Peptoid Oligomers. In the course of this study, we have created a series of 20 different peptoid oligomers of varying length and sequence, based on the monomers carrying the side chains shown in Table 1. N-substituted glycine oligomers comprising 3 to 20 monomers were synthesized in good yield and crude purity, estimated by analytical reversed-phase HPLC and electrospray mass spectroscopy. In all cases, purities and molar masses of HPLC-purified samples were confirmed by analytical reversed-phase HPLC and electrospray mass spectroscopy. In all cases, masses were consistent with expected values (Table 2).

Since we wished to study and compare the secondary structure of a large number of different peptoid sequences composed of the same or similar side chains, CD was the most practical tool to be used. Full structure determination by multidimensional NMR is challenging for these particular peptoid homooligomers due to extensive spectral overlap. Moreover, as has been reported for oligoprolines and proline-rich oligomers taken out of the context of folded proteins,24,25 we have found it difficult to grow high-quality crystals of the organosoluble Npe oligomers described in this study; this effort is ongoing. For polyprolines, lack of access to crystal structures has led to extensive use of CD24,25 and vibrational CD,26 as well as careful comparison of these CD spectra to theoretical calculations27–31 to provide deeper understanding of their secondary structure.

CD is a useful tool for the assessment and classification of folded structure in peptides and proteins because the amide bond chromophore is acutely sensitive to the structural, electronic, and solvation environment in which it lies. A rich literature exists on the topic of CD spectrum interpretation for polypeptides, and characteristic peaks and valleys in ellipticity are assigned to α-helices, β-sheets, β-turns, and other helical conformers found in peptides and proteins, including polyproline type I and II helices.32 For oligopeptides with α-chiral, aromatic side chains, the correlation of intense CD spectra with the existence of helical secondary structure in solution has been supported by both NMR and molecular modeling studies.17,21,23

As a point of reference, the CD of an oligomer of achiral Npm residues (1) exhibits no net ellipticity (see Supporting Information), indicating the lack of a single, dominant chiral structure in acetonitrile solution in the absence of chiral side chains. In the absence of an ordered backbone conformation, the aromatic groups on the side chains exhibit no net CD. Additionally, we confirm the finding of Kirshenbaum et al.17 that despite the achirality of the peptoid backbone and its absence of hydrogen bond donors, oligopeptides with α-chiral side chains will populate a helical conformer with a handedness dictated by the chirality of the side chains. Specifically, we find that peptoid hexamers 2 and 6 with aromatic, α-chiral (S or R) side chains show perfect “mirror image” helical CD spectra in acetonitrile solution (see Supporting Information and Figure 1a).

Given that peptoids share the same backbone structure as peptides and that backbone amide groups are also the predominant chromophores in peptoids, we consider it useful to invoke accepted interpretations of polypeptide CD22,33 to interpret peptoid CD spectra. In the standard interpretation for peptides, the band displayed by oligomer 6 at 218 nm is taken to correspond to the ππ* transition of the amide chromophore, typically occurring between 230 and 210 nm in peptides depending upon solvent conditions. The bands at 202 and 192 nm reflect high and low wavelength components of the exciton-split ππ* transition, typically occurring around 200 nm in tertiary amides.22,33 Additional, side chain-related contributions to the spectra in the UV region may include coupled interactions between peptide amide transitions and the πτ transition of the aromatic side chains, occurring at ~210 nm for phenylalanine in polypeptides, which are most often observed to be weakly positive in sign for natural L-peptides.34 The consequence of the appearance of these positive CD bands in the spectra of phenylalanine-containing proteins and peptides is that the average helicity may be underestimated. Considering peptoid helix 2, which has the same handedness as a natural L-peptide helix and gives a mirror-image spectrum to that of 6 (Figure 1a), a positive contribution from coupled amide-πτ transitions may be the source of a weak local maximum occurring at 210 nm, perhaps deepening the cleft observed in the “double minimum” (see Supporting Information). The definitive source

Figure 1. A comparison of the CD spectra of Npe peptoid oligomers as a function of chain length: (a) oligomers 5, 6, 7, and 8; (b) oligomers 8, 9, 10, 11, and 12; and (c) oligomers 12, 13, 15, 18, and 20. Peptoid concentration was ~60 μM in acetonitrile; spectra were acquired at room temperature.

We have carefully investigated the possibility that helical structures giving rise to intense CD spectra such as that of 6 might result from intermolecular association. For example, we considered the possibility of a π-π stacking interaction between aromatic side chains on interdigitated, antiparallel peptoid oligomers. CD spectra were acquired for compound 6 at seven different concentrations between 0.8 and 64 μM (see Supporting Information). We found little difference in the shape or intensity of the spectra over this almost 100-fold range in concentration. This indicates that peptoid helices of this class are unlikely to be stabilized by intermolecular association in the concentration region in which CD spectra were acquired (~60 μM). Hence, we attribute the strong CD that we observe for these peptoids to the adoption of repeating secondary structure by the backbones of individual peptoid helices.

Homooligomer Structure as a Function of Chain Length.

To determine the effect of chain length on the formation of chiral secondary structure, a one-by-one length series of peptoid homooligomers with aromatic, α-chiral Npe side chains was synthesized, purified, and characterized by CD in acetonitrile solution. Relatively strong CD signatures are observed even for the trimer 3 and tetramer 4 (see Supporting Information). Characteristic spectral features described previously for the CD spectrum of 6 (Figure 1a) are echoed in these short oligopeptides, but are weaker and less well-defined. In comparison with 3 and 4, the Npe pentamer 5 (Figure 1a) exhibits strong CD with well-defined peaks at 192, 202, and 218 nm. The spectra of Npe oligomers ranging in length from a pentamer to a 20mer are compared in Figure 1a—c. As shown in Figure 1a and in previous work,17,23 stable helical structures are obtained for peptoids as short as five residues in length, while protohelical structures are observed at a trimer and tetramer length. This finding is consistent with previous observations of oligoprolines, which also have been observed to form protohelical structures at a trimer length.24 As suggested in previous work with β-peptides,35,36 these results confirm that avoidance of steric clash creates a powerful driving force for the adoption of secondary structure even in very short oligomers.

An intriguing dependence of CD on chain length is seen for oligomers 5, 6, 7, and 8, where similarly shaped spectra are decreased in intensity with each added monomer (Figure 1a). The presence of a clear isodichroic point at 196 nm is evidence of a self-consistent decrease in the overall percentage of helical (Npe)ₙ conformers, as chain length is increased from 5 to 8 residues. For polypeptides, the presence of an isodichroic point near 200 nm is considered to be diagnostic for a two-state helix-coil transition, though it is relatively unusual for this transition to occur as a function of chain length.37

Extrapolating from previously accumulated knowledge about the preferred solution structures of Npe peptoid oligomers, we hypothesize that in Npe 5–8mers there is a length-dependent shift in the relative population of cis-amide helices and an alternate family of conformers that has at least one, carboxy-terminal trans-amide bond.23 We base this prediction on the solution structure of an Npe pentamer (with p-benzyl substituents), which was shown by 2D-NMR to preferentially adopt a right-handed helix with a cis-amide bond, and yet to have a

minor population of conformers containing one or more trans-amide bonds. Modeling suggested that the amide bond of the second-to-last residue on the carboxy terminus of the peptoid (residue 4 in the pentamer) might have a particular reason for locally favoring the trans isomer. In particular, this geometry allows the C-terminal amide hydrogens of the carboxamide tail to hydrogen bond with the carbonyl oxygen of residue 4, if residues 2–4 adopt the dihedral angle values of the major isomer observed by NMR.\textsuperscript{11,23}

Interconversion of predominantly cis-amide conformers with another family of conformers having one or more trans-amide bonds may be increasingly favored as chain length is increased from five to eight residues. This is supported by previous modeling and NMR structural studies for chiral, \textit{para}-substituted aromatic peptoids, which showed that the free energy barrier of \textit{cis}–\textit{trans} isomerization of backbone amide bonds in peptoids is relatively low in comparison to that of peptides.\textsuperscript{23} The presence of a sharp isodichroic point for the spectra of 5–8 would seem to indicate that the transition from one peptoid structure to another occurs cooperatively or is at least self-consistent in this set of oligomers. This is consistent with studies of chiral \textit{m}-phenylene ethylene oligomers, where the presence of an isodichroic point in the CD spectra has been suggested to imply that the side chains of the oligomers cooperatively interact, producing an increased twist sense bias as a function of chain length.\textsuperscript{38}

Continuing in the length series, the spectra of \textit{Nrpe} nonamer 9 and decamer 10 are compared with that of octamer 8 in Figure 1b. In comparison to the spectra of shorter \textit{Nrpe} oligomers, the spectrum observed for nonamer 9 is qualitatively different, with significantly more intense CD peaks in the 195–230 nm range. An apparent coalescence and blue-shifting of the two CD maxima observed in shorter \textit{Nrpe} oligomers yields a broad, shouldered peak that is centered at 203 nm and exhibits an ellipticity almost three times the strength of the signal for 8 in that range of wavelengths. The CD signature of 9 appears to be unique, as the spectrum of the decamer 10 reverts to a shape and intensity similar to that of 8, though significantly stronger in intensity (Figure 1b). The comparison of the CD spectra of the nonamer 9 with both shorter and longer chains suggests that the alternative secondary structure adopted by the nonamer 9 is meta-stable with chain length.

Undecamer 11 and dodecamer 12 again exhibit distinct CD spectra in comparison to oligomers with just one or two fewer monomers. In comparison to decamer 10, the spectra of 11 and 12 are characterized by \textasciitilde 40% greater intensity of the negative peak at 192 nm and \textasciitilde 50% lower intensity of the positive peak at 204 nm (Figure 1b). Spectra for 11 and 12 are virtually superimposable. If there are some aspects of cooperativity in the stabilization of peptoid secondary structure, then it would make sense that as chain length increases, the most stable conformer increasingly predominates. On the basis of this line of reasoning, we hypothesize that at the undecamer chain length, the conformer with one or more trans-amide bonds ceases to make a significant contribution to the mixed population of secondary structures.

As the number of \textit{Nrpe} peptoid oligomers is raised from 12 to 13, we observe another 50% increase in CD signal intensity (Figure 1c). This increase in CD ellipticity as a function of chain length has also been observed for chiral \textit{m}-phenylene ethylenylene oligomers.\textsuperscript{38} For longer \textit{Nrpe} oligomers, the shapes and intensities of the CD spectra are highly similar (spectra of 12, 13, 15, 18, and 20 are shown). CD spectra for 18, 19, and 20, in particular, are perfectly super-imposable and extremely intense (data for 19 not shown). For these longer \textit{Nrpe} peptoid oligomers, the peak at 204 nm appears as a relatively small shoulder on a much more intense peak at 222 nm. The intensity and wavelength dependence of peptoid \textit{Nrpe} CD spectra reaches a plateau for the 13mer, and no further significant changes are noted for longer chains up to the 20mer. This length-dependent stabilization of CD spectral shape and intensity is consistent with CD observations of isolated oligopeptides in solution. For peptides, it is typically observed that the intensity of a helical CD signal (particularly the band at \textasciitilde 190 nm) increases as a function of chain length until it reaches maximal intensity at around 15 residues, depending upon the peptide monomer sequence and solvent conditions.\textsuperscript{39} The requirement for a certain minimum number of peptide residues for achievement of helical stability is evidence of the cooperation of the monomer units in stabilizing the helix. Our observations of peptoid CD as a function of chain length lead us to hypothesize that peptoid helix formation, at least for \textit{Nrpe} oligomers, is also a cooperative process. We believe that when an oligomer length of 11–13 residues is reached, a helix with \textit{cis}-amide bonds becomes the most favored conformation by a sufficiently wide free energy margin that contributions to the CD from \textit{trans}-amide-containing conformers (at about 203 nm) cease to affect spectral shape and intensity. We hypothesize that the conformations adopted by these longer oligomers are similar to that previously observed for the major conformers in the \textit{Nrpe} pentamer, which are right-handed with \textit{cis}-amide bonds, having a periodicity of about three residues per turn and a pitch of \textasciitilde 6 Å.\textsuperscript{23}

\textbf{The Effect of Temperature on Hexamer, Dodecamer, and Octadecamer Helices.} The effect of temperature elevation on the helical stability of peptoids 6, 12, and 18 was investigated by CD. As can be seen in Figure 2, the dodecamer 12 shows only a small reduction in ellipticity and no change in shape as temperature is increased from 5 to 75 °C, implying that these

\begin{figure}[h!]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{The effect of temperature on the CD spectra of \textit{Nrpe} oligomer 12. Spectra were acquired between 5 and 75 °C in 10° increments; results for only five temperatures are shown, for clarity. Sample concentration was \textasciitilde 60 \mu M.}
\end{figure}


peptoid helices are quite stable to thermal unfolding. The spectra taken at 65 and 75 °C are superimposable, indicating that the disordering transition is complete at 65 °C. The thermal behavior of 6 and 18 (see Supporting Information) is very similar to that of 12. These results are consistent with work by Kirshenbaum et al.\textsuperscript{17} on the thermal stability of peptoid helices and are expected in light of the absence of hydrogen-bonding stabilization of the helix. Steric driving forces for helical ordering are less likely to be disrupted by increased temperature than are hydrogen-bonding, electrostatic, or hydrophobic driving forces.\textsuperscript{40–42}

Interestingly, CD spectra taken at eight different temperatures (of which only five are shown, for clarity) pass through isodichroic points for all three oligomers, at 196 and 224 nm for 6 and 198 and 232 nm for 12 and 18. This suggests that the minor structural destabilization, either from a more ordered to a less ordered helix or from one predominant secondary structure to another, occurs in a cooperative fashion.

Three Different Classes of Peptoid Secondary Structure as a Function of Npe Chain Length. Figure 3 allows a comparison of the three different classes of CD spectra that are displayed by Npe oligomers, plotted over the same range of ellipticity so that the striking differences in their relative shapes and intensities are easily seen. Characteristic spectra of Npe hexamer 6, nonamer 9, and 20mer 20, each of which display distinct and proto-typical CD signatures, are shown in the figure. Allowing for chain length-dependent differences in intensity, the CD spectra of oligomers 4, 5, 7, 8, and 10 are similar to that of 6, whereas the spectrum of oligomer 9 is unique, and the spectra of oligomers 11–19 closely resemble that of 20.

We believe that the relative population of conformers with cis- and trans-amide bonds in the peptoid backbone gives rise to these different classes of chiral secondary structures. Ongoing 2D-NMR studies of these peptoids support the hypothesis that the conformations adopted by peptoids are chain-length dependent for short oligomers and only become independent of length after a minimal number of residues (11–13 Npe monomers).\textsuperscript{1}H–\textsuperscript{13}C HSQC spectra of α-chiral, aromatic and aliphatic peptoids clearly reveal the presence of different conformer populations at chain lengths of 6, 9, and 15 monomers (data not shown, manuscript in preparation). Through further studies by 2D-NMR (TOCSY, TROESY, and HMBC) and crystallography, we are working to uncover the specific structural differences that give rise to this rich variation in the CD signatures of peptoid oligomers with α-chiral, aromatic side chains.

Conclusions

This detailed, comparative study of 20 different peptoid oligomers has yielded a better understanding of how chain length impacts the chiral secondary structures that they can adopt, but has also raised a number of new questions. A few results for this system are very clear: Peptoids with α-chiral, aromatic side chains form helical secondary structure, even in chains as short as a pentamer. Helical sense is dictated by the handedness of the side chains, and helix formation in peptoids is not dependent upon intermolecular association. As yet unexplained is the striking evolution in CD signatures for Npe chains 4 through 12 residues in length, which is particularly interesting for pentamer 5 through nonamer 9. The nonamer adopts a distinct, and as yet uncharacterized, secondary structure that appears to differ fundamentally from that of other peptoid oligomers. The oligo-Npe secondary structures are stable up to 75 °C. The secondary structure of peptoid helices becomes length-independent for chains longer than 12 residues. Through further 2D-NMR and crystallographic studies, we are presently working to obtain a more complete understanding of the helical structures adopted by peptoid chains that include aromatic, α-chiral side chains. We hope that this deepened understanding of chiral peptoid helices will eventually lead to their use as therapeutic agents or as novel biomaterials, both as isolated helices and as elements of larger biomimetic structures.

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Supporting Information Available: CD spectra of peptoid oligomers 1, 2, 3, 4, 5, 6, and 18 (PDF). This material is available free of charge via the Internet at http://pubs.acs.org. JA003153V